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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.

THE PREPARATION OF SODIUM PHOSPHOMOLYBDATES FROM MOLYBDIC ANHYDRIDE AND SODIUM PHOSPHATES

E. A. Nikitina and E. V. Buris

It is indicated in the literature [1] that sodium phosphomolybdate of composition $Na_2H_5[P(Mo_2O_7)_6] \cdot xH_2O$ can be obtained from molybdic acid and disubstituted sodium phosphate. However, the conditions for running the reaction have been left completely undeveloped and the proposed starting material – molybdic acid – is poorly suitable for synthetic purposes, since it always contains undesirable NH_4^+ impurity. Consequently, our task was to develop a method for the synthesis of sodium phosphomolybdate from crystalline molybdic anhydride, failing to contain ammonium salt impurities.

EXPERIMENTAL

The starting substance – crystalline molybdic anhydride – was prepared by the ignition of ammonium paramolybdate of apothecary grade, as had been described in detail earlier [2].

The obtained crystalline molybdic anhydride was dissolved in a water solution of disodium phosphate in accord with the equation:

$$12MoO_3 + Na_2HPO_4 + 2H_2O \rightleftharpoons Na_2H_5[P(Mo_2O_7)_6].$$

The indicated complex-formation reaction is reversible, and our problem was to establish the conditions under which it proceeded most completely in the desired direction.

The experiments run by us, revealed that it is most expedient to run the complex-formation process at the boiling point. To obtain the maximum yield of sodium phosphomolybdate, it is helpful to use an excess of molybdic anhydride. It was experimentally established that the excess of molybdic anhydride should not exceed 200% of the stoichiometric amount. A smaller amount of molybdic anhydride lowered the yield of sodium phosphomolybdate, while an ever larger excess no longer increased the yield.

The process for obtaining the sodium phosphomolybdate was run under the following conditions: into a 2-liter round-bottomed flask was charged 780 g of molybdic anhydride, 80.8 g of disodium phosphate and 1 liter of water. The reaction mixture was stirred with a mechanical stirrer and boiled for 1.5 hours. During the boiling process, the solution acquires an intensely yellow color, characteristic for the $[P(Mo_2O_7)_6]^{VII}$ ion. Water is not added during the complex-formation process, and consequently, on conclusion of heating the sodium phosphomolybdate solution is close to the saturated state; its specific gravity at 20° reaches 1.6-1.7, while the volume is about 350 ml.

After cooling, the sodium phosphomolybdate solution was filtered from excess molybdic anhydride. The unreacted molybdic anhydride was used in subsequent syntheses.

The obtained concentrated solution of sodium phosphomolybdate was evaporated in a porcelain dish, either on the water bath or over a gas burner with asbestos gauze at slight boil, until a crystalline film formed on the solution surface, and then it was cooled to room temperature. The resulting crystals were filtered and either dried in the air, or in a drying oven at about 40°; the yield of the first fraction of disodium phosphomolybdate was 70%; the filtrates from the isolation of the first fraction of crystals were combined from several batches, and then evaporated to obtain more crystals; in this way the yield of the salt rose to 80-85%.

Analysis of the obtained salt preparations revealed that their composition corresponded to the disubstituted salt, contaminated in some cases with the trisubstituted salt (see Table).

Analysis of Sodium Phosphomolybdate Calculated on the Anhydrous Composition.

		Na_2O	P_2O_5	MoO_3
Calculated				
Disubstituted salt		3.10	3.51	93.39
Trisubstituted salt		4.91	3.68	91.41
Found				
Disubstituted salt	(I)	3.63	3.42	92.95
	(II)	3.25	—	—
Trisubstituted salt	(III)	4.87	3.81	91.32
	(IV)	4.95	3.80	91.25

Remarks. The analysis of the obtained salts consisted in determining the H_2O, Na_2O and P_2O_5, as had been described earlier [3]. The amount of MoO_3 was calculated by difference.

The trisodium phosphomolybdate was obtained by the reaction:

$$12MoO_3 + Na_3PO_4 + 2H_2O \rightleftharpoons Na_3H_4[P(Mo_2O_7)_6].$$

For 800 g of MoO_3 we took 90 g of trisodium phosphate. Here the running of the complex-formation reaction proved to be more complicated; frequently the reverse process was observed here, i. e., decomposition of the heteropoly anion, due to the somewhat greater alkalinity of the Na_3PO_4 solution. It is possible to obtain a crystalline trisodium phosphomolybdate, free of decomposition products as impurities, only if solutions with d 1.7 are taken for crystallization. Here it also proved expedient to recrystallize the obtained salt once from water (100 ml of water should be taken per 100 g of trisodium phosphomolybdate). Here the yield of heteropoly salt was also 70% in the first fraction; evaporation of the filtrates raised the yield to 80-85%.

The proposed method for the preparation of the sodium phosphomolybdates is relatively simple when compared with those described in the literature [3]; it makes it possible to achieve a fairly complete treatment of the taken MoO_3, assures a good yield, and permits avoiding numerous (3-4 times) recrystallizations and the use of organic solvents for extracting the heteropoly salts.

SUMMARY

1. A method was developed for obtaining disodium phosphomolybdate from MoO_3 and Na_2HPO_4.

2. A method was developed for obtaining trisodium phosphomolybdate from MoO_3 and Na_3PO_4.

3. The yields of the salts reach 70% in the first fraction. By using the filtrates from the first fraction, the yield of the salts is raised to 80-85%.

4. The developed methods possess an advantage over earlier known methods in view of their greater simplicity and excellent yield.

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*T.p. = C. B. Translation pagination.

STUDY OF THE MELTS OF POTASSIUM AND SILVER NITRATES BY THE METHOD OF ELECTROMOTIVE FORCES

M. S. Zakharyevsky and T. V. Permyakova

According to the data of Y. Doucet and Le Duc [1, 2], the $KNO_3 - AgNO_3$ system is ideal in the whole temperature interval and its fusion diagram shows a eutectic without the formation of compounds. According to the data of Ussow [3], the studied system shows the formation at low temperatures of a chemical compound with incongruent melting point, i. e., the system behaves like a nonideal system. The data of these authors were obtained by the thermal analysis method. Based on the ionic nature of molten salts, electrochemical methods can be used for their study.

The data of [4] show that a study of the emf of concentration chains gives the most complete and reliable information relative to complex-formation in fused salts, for which reason this study method was chosen in the present investigation.

EXPERIMENTAL

Measurement Method

To study the system $KNO_3 - AgNO_3$ we utilized a study of the concentration chain

$$Ag \left| \begin{array}{c|c} AgNO_3 & AgNO_3 \\ N_1 & N_1' \\ KNO_3 & KNO_3 \\ N_2 & N_2' \end{array} \right| Ag.$$

We utilized the method developed by Gordon [5], Lorenz [6], and others: the studied melt was placed in the cell, terminating in a capillary end, and the cell in turn was placed in the crucible with intermediate electrolyte. To avoid permeation of the intermediate electrolyte from crucible into the electrode vessel, the level of the melt in the latter was kept as exactly as possible at the level of the intermediate electrolyte.

When the $KNO_3 - AgNO_3$ mixture is melted in the electrode vessel itself, an air bubble frequently forms in the capillary, which can be removed only with difficulty. To avoid this, a glass triangle was inserted in the stopper of the cell, through one opening of which a silver electrode was introduced, while the second opening was connected through a rubber tube with a micropump. The studied $KNO_3 - AgNO_3$ mixture (previously fused and crushed to a powder) was melted in the crucible, mixed by blowing with air, and then sucked into the electrode vessel with the aid of the micropump. After this, the electrode vessel was placed in the crucible with intermediate electrolyte. The second electrode vessel was filled with the melt in a completely analogous manner.

The electromotive forces were measured at constant temperature in the interval 135-320°. A massive heat block, made of silumin and weighing 34 kg, served as the thermostat. Externally and underneath, the heat block was heat-insulated with a layer of asbestos 3 cm in thickness. A rheostat was used to maintain the temperature constant to within 1°.

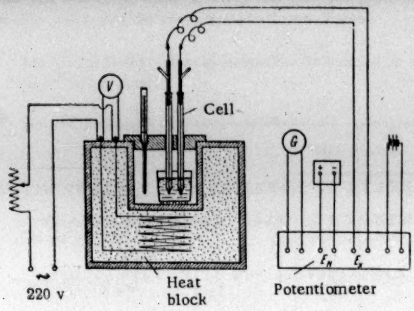

Fig. 1. Diagram of the apparatus.

As electrodes we used silver wires with copper leads. Prior to operation, the electrodes were rinsed with hot distilled water and then dried with filter paper. Control experiments were set up to check the reversible nature of the electrodes: the electrodes were immersed in the same melt, containing silver ions. An electromotive force failed to develop over a prolonged period of time. The reproducibility of the results when operating with such electrodes was of the order of 1 mv.

The compensation method was used to measure the electromotive forces. A diagram of the apparatus is shown in Fig. 1.

Decomposition of the $AgNO_3$ occurs during the time of running the experiment (the melt darkens in approximately 30-40 minutes after starting the experiment), for which reason fresh solutions were prepared for each experiment.

Measurement Results

The $KNO_3 - AgNO_3$ system was studied at 320, 250, 200, 180, 150, 140 and 135°.

We ran two series of experiments. The first series of experiments was run to determine if the studied system is ideal in the whole concentration interval at the given temperatures, and also to obtain some idea as to the diffusion potential. The measurement results are presented in Table 1.

The second series of experiments was run for the purpose of verifying whether the system is ideal close to the eutectic point. For this, a melt with composition (in mole percent) 0.556 $AgNO_3$ and 0.444 KNO_3 (eutectic composition, based on the fusion diagram of Doucet and Le Duc) was placed in one electrode vessel; solutions of $AgNO_3$ in KNO_3 of various concentration were placed in the second electrode vessel. The results of these experiments are presented in Table 2.

DISCUSSION OF RESULTS

The emf of an ideal concentration chain with concentration ratio $\frac{N_1'}{N_1}$ is

$$E_1 = 9 \log \frac{N_1'}{N_1}.$$

The emf of a concentration chain with concentration ratio $\frac{N_1''}{N_1}$ is

TABLE 1

Temperature	Concentration ratio KNO_3 : $AgNO_3$	E (mv) measured	E (mv) theoretical	ΔE (mv)
320°	0.3 : 0.1	+57.3	+56.6	—0.7
320	0.6 : 0.1	+93.0	+92.3	—0.7
320	0.2 : 0.1	+36.5	+35.7	—0.8
320	0.5 : 0.2	+48.0	+47.2	—0.3
320	0.6 : 0.4	+20.4	+20.9	+0.5
320	0.7 : 0.5	+16.9	+17.3	+0.4
320	0.9 : 0.6	+20.1	+20.8	+0.7
250	0.9 : 0.6	+18.1	+18.4	+0.3
250	0.9 : 0.4	+37.2	+36.8	—0.4
150	0.65 : 0.47	+ 7.0	+11.9	+4.9
140	0.61 : 0.5	+ 0.8	+ 7.1	+6.3
135	0.6 : 0.52	— 2.3	+ 5.1	+7.4

TABLE 2

Temperature	Concentration ratio KNO_3 : $AgNO_3$	E (mv) measured	E (mv) theoretical	ΔE (mv)
320°	0.1 : 0.556	—89.3	—88.4	+0.9
320	0.2 : 0.556	—52.6	—52.6	0.0
320	0.3 : 0.556	—31.7	—31.8	—0.1
320	0.4 : 0.556	+17.4	—16.9	+0.5
320	0.7 : 0.556	+11.7	+11.9	+0.2
320	0.8 : 0.556	+18.6	+18.7	+0.1
320	0.9 : 0.556	+24.6	+24.8	+0.2
250	0.3 : 0.556	—28.8	—28.0	+0.8
250	0.4 : 0.556	—15.7	—15.0	+0.7
250	0.47 : 0.556	—8.1	— 7.6	+0.5
250	0.65 : 0.556	+ 6.8	+ 7.1	+0.3
250	0.7 : 0.556	+10.7	+10.5	—0.2
250	0.8 : 0.556	+16.0	+16.4	+0.4
200	0.47 : 0.556	— 6.5	— 6.9	—0.4
200	0.65 : 0.556	+ 6.4	+ 6.5	+0.1
180	0.47 : 0.556	— 5.7	— 6.6	—0.9
180	0.65 : 0.556	+ 5.5	+ 6.1	+0.6
150	0.65 : 0.556	+ 3.2	+ 5.8	+2.6
150	0.47 : 0.556	— 3.3	— 6.2	—2.9
150	0.5 : 0.556	— 1.3	— 3.9	—2.6
150	0.53 : 0.556	— 0.2	— 1.8	—1.6
140	0.5 : 0.556	— 0.8	— 3.8	—3.0
140	0.61 : 0.556	0.0	+ 3.3	+3.3
140	0.51 : 0.556	— 0.3	— 3.1	—2.8
140	0.53 : 0.556	0.0	— 1.7	—1.7
135	0.6 : 0.556	— 1.3	+ 2.7	+4.0
135	0.52 : 0.556	+ 1.0	— 2.4	—3.4
135	0.58 : 0.556	— 1.6	+ 1.5	+3.1
135	0.53 : 0.556	+ 0.8	— 1.7	—2.5

$$E_2 = \vartheta \log \frac{N_1''}{N_1}.$$

From this it follow that the emf of a concentration chain with concentration ratio $\frac{N_1'}{N_1''}$ is equal to

$$E_{calc.} = E_1 - E_2 = \vartheta \log \frac{N_1'}{N_2''}.$$

The reproducibility of the experimental results can be checked by subtracting from each other the corresponding emf values of the second series of experiments and comparing the obtained values with the emf values of the first series of experiments. Here it is necessary to limit ourselves to that temperature region where chemical reaction between the solution components fails to be observed.

Such a comparison of the calculated and experimentally determined emf values indicates that the reproducibility of the experimental results is fully satisfactory within the limits of 1 mv (Table 3).

TABLE 3

Concentration ratio KNO_3: $AgNO_3$	E_3 (from 1st series of expts)	$E_{calc.}$ (from 2nd series of expts)	ΔE
0.3 : 0.1	57.3	57.6	0.3
0.2 : 0.1	36.5	36.7	0.2

Since an increase in the concentration interval (0.2 : 0.1 = 2 and 0.6 : 0.1 = 6) failed to introduce essential changes in the measured emf values (Table 1), it can be concluded that the diffusion potential failed to exceed the measurement error.

We will now compare the experimentally obtained emf values with those calculated by the Nernst formula:

$$E_{theor} = \vartheta \log \frac{N_1'}{N_1}.$$

In their nature fused salt mixtures are very close to completely ionic solutions, where chemical reaction between the solution components fails to occur [7-9]. Consequently, a comparison of the measured values of the emf of a concentration chain $E_{measured}$ with those calculated by the Nernst formula $E_{theor.}$ can characterize the deviation degree of the system from ideality.

Strictly speaking, the emf method does not permit judging as to the nature of the reaction products formed in solution (whether they are molecules or complex ions) but only shows in what ratio the starting components react, if the system is nonideal. Consequently, speaking in the future of the composition of the formed "compound" we will have in mind specifically, the ratio of the reacting components, irrespective of the nature of the products formed as a result of this reaction.

The fact that the value $\Delta E = E_{theor.} - E_{measured}$ is not equal to zero only indicates that actually there is reaction between the solution components.

From Tables 1 and 2 it can be seen that above 150° the $KNO_3 - AgNO_3$ system acts as though it were ideal (the differences between the calculated and measured emf values lie within the measurement error of ± 1 mv).

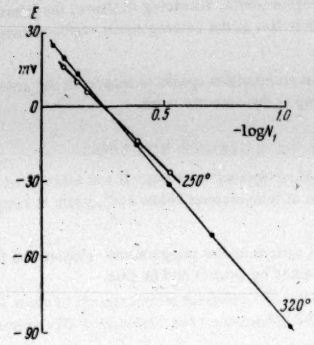

Fig. 2. Dependence of the emf of the concentration chains on the composition of the solution.

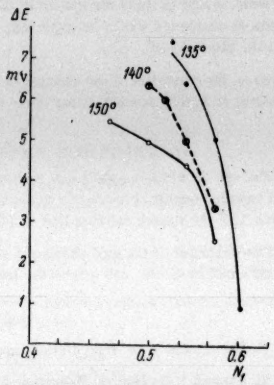

Fig. 3. Diagram of the dependence of the deviations in the experimental emf values from those calculated according to the Nernst equation on solution composition.

At elevated temperatures a good linear-logarithmic relationship is observed between the emf and log N (N_1' = const = 55.6 mole % $AgNO_3$). This relationship is depicted in Fig. 2. The relationship begins to show noticeable deviation from linearity below 150°, in which connection this deviation increases with decrease in temperature.

In all of the experiments (at 150, 140 and 135°) the emf of the concentration chains were measured at a constant concentration, and specifically at N_1 = 55.6 mole % $AgNO_3$, N_2 = 44.4 mole % KNO_3 (the eutectic composition according to Doucet and Le Duc).

The emf of the concentration chains were calculated on the basis of equation (a) from the experimentally determined values of emf at these temperatures.

The calculation results are presented in Table 4. The emf of the chains, calculated by the Nernst equation ($E_{theor.}$), and the difference $\Delta E = E_{theor.} - E_{calcd.}$, are also presented in the same table.

TABLE 4

Temperature	Concentration ratio $KNO_3 : AgNO_3$	E(mv) measured	E(mv) theoretical	ΔE (mv)
150°	0.65 : 0.556	+3.2	+ 5.7	+2.5
150	0.65 : 0.5	+4.5	+ 9.6	+5.1
150	0.65 : 0.47	+6.5	+11.9	+5.4
150	0.65 : 0.53	+3.0	+ 7.4	+4.4
140	0.61 : 0.556	0.0	+ 3.3	+3.3
140	0.61 : 0.51	+0.3	+ 6.4	+6.1
140	0.61 : 0.5	+0.8	+ 7.1	+6.3
140	0.61 : 0.53	0.0	+ 5.0	+5.0
135	0.6 : 0.58	+0.3	+ 1.2	+0.9
135	0.6 : 0.556	−1.3	+ 3.8	+5.1
135	0.6 : 0.52	−2.3	+ 5.1	+7.4
135	0.6 : 0.53	−2.1	+ 4.3	+6.4

The relationship between ΔE and the solution composition is depicted in Fig. 3.

We were unable to study the system in the concentration region where, according to Ussow, the formation of a chemical compound was to be expected, since such a mixture lies in the heterogeneous region at temperatures of 150, 140 and 135°.

However, the character of the changes in ΔE with change in composition speaks in support of the presence of compounds at $AgNO_3$ concentrations lower than that prevailing at the eutectic point.

SUMMARY

1. The system $KNO_3 - AgNO_3$ was studied by the method of electromotive forces. It was established that chemical reaction occurs between the components of the system at temperatures below 150°, while at temperatures above 150° the system behaves like an ideal system.

2. The character of the emf changes in the $KNO_3 - AgNO_3$ system at low temperatures supports the fusion diagram obtained by Ussow, and refutes the fusion diagram presented by Doucet and Le Duc.

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SURFACE TENSION OF BINARY SYSTEMS COMPOSED OF ACETIC ACID AND ITS CHLORO DERIVATIVES

I. M. Bokhovkin

A study of the electroconductivity, viscosity, density and surface tension of binary systems, formed by acetamide with acetic acid and its chloro derivatives, is described in [1-4].

The present investigation is devoted to a study of the fusibility and surface tension in binary systems composed of acetic acid and its chloro derivatives.

The starting substances were first purified before use: the acetic acid by freezing, and the monochloroacetic, dichloroacetic and trichloroacetic acids by a double distillation. Their melting points were close to those given in the literature [5].

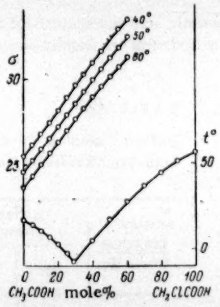

Fig. 1. Fusibility diagram and surface tension isotherms in the binary system acetic acid-monochloroacetic acid.

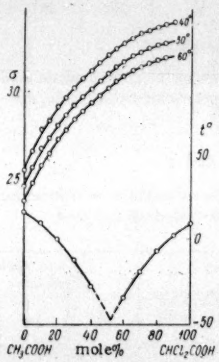

Fig. 2. Fusibility diagram and surface tension isotherms in the binary system acetic acid-dichloroacetic acid.

Rebinder's method [6] was used to determine the surface tension. The method is discussed in detail in [7]. The apparatus, in which the surface tension determinations were made, was immersed in a water thermostat, in which a constant temperature was maintained by means of a mercury-toluene thermoregulator. The fusibility was studied by the visual-polythermal method. The composition was expressed in mole percent.

A study of the fusibility of mixtures of acetic acid with its chloro derivatives indicates that interaction between the components is absent [8].

The fusibility diagrams obtained by us for the three binary systems are shown in Figs. 1-3. They are all characterized by having a simple eutectic.

We studied the surface tension of all three systems at 40, 50 and 60°. In the first system, the curves were made up to 60% monochloroacetic acid, in the second up to 90% dichloroacetic acid, and in the third system, up to 50% trichloroacetic acid. The experimental data on determining the surface tension are summarized in Tables 1-3. The surface tension isotherms are shown in Figs. 1-3.

TABLE 1

Surface Tension in the System Acetic Acid-Monochloroacetic Acid

Amount of $CH_2ClCOOH$ (mole %)	Surface tension (dynes/cm)		
	40°	50°	60°
5	26.2	25.3	24.4
10	26.8	25.9	25.1
15	27.4	26.5	25.7
20	28.2	27.3	26.8
25	28.9	28.0	27.0
30	29.7	28.6	27.7
35	30.4	29.3	28.4
40	31.0	30.1	29.0
45	31.7	30.7	29.6
50	32.5	31.4	30.3
55	33.1	32.0	30.8
60	36.6	32.7	31.4

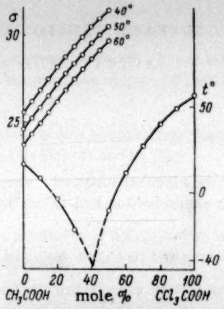

Fig. 3. Fusibility diagram and surface tension isotherms in the binary system acetic acid-trichloroacetic acid.

They are ~ linear in the systems acetic acid-monochloroacetic acid and acetic acid-trichloroacetic. In the system acetic acid-dichloroacetic acid, the surface tension isotherms are slightly convex to the composition

TABLE 2

Surface Tension in the System Acetic Acid-Dichloroacetic Acid

Amount of $CHCl_2COOH$ (mole %)	Surface tension (dynes/cm)		
	40°	50°	60°
15	28.5	27.5	26.6
20	29.2	28.1	27.3
25	29.7	28.7	27.9
30	30.3	29.2	28.5
35	30.8	29.8	29.0
40	31.3	30.3	29.5
45	31.8	30.7	30.0
50	32.3	31.2	30.4
55	32.7	31.6	30.7
60	33.0	31.9	31.0
65	33.3	32.2	31.4
70	33.6	32.5	31.7
75	33.8	32.7	31.9
80	34.0	32.9	32.1
85	34.2	33.2	32.3
90	34.3	33.4	32.5

TABLE 3

Surface Tension in the System Acetic Acid-Trichloroacetic Acid

Amount of CCl_3COOH (mole %)	Surface tension (dynes/cm)		
	40°	50°	60°
5	26.2	25.1	24.3
10	26.9	25.9	24.9
15	27.5	26.6	25.6
20	28.2	27.2	26.2
25	28.8	27.9	26.9
30	29.5	28.5	27.6
35	30.1	29.1	28.2
40	30.7	29.7	28.7
45	31.1	30.2	29.3
50	31.6	30.7	29.8

axis. This character of the curves for the surface tension isotherms of the binary systems composed of acetic acid and its chloro derivatives, the same as the fusibility diagram, fails to give any indications of the presence of definite chemical compounds in the molten homogeneous medium.

SUMMARY

1. The surface tension values of the binary systems $CH_3COOH - CH_2ClCOOH$, $CH_3COOH - CHCl_2COOH$ and $CH_3COOH - CCl_3COOH$ were measured at 40, 50 and 60°.

2. Chemical interaction of the components was not shown in the indicated systems.

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PHYSICOCHEMICAL ANALYSIS OF BINARY SYSTEMS FORMED BY ACETAMIDE WITH ORGANIC ACIDS

IV. SURFACE TENSION OF BINARY SYSTEMS FORMED BY ACETAMIDE WITH ACETIC ACID AND ITS CHLORO DERIVATIVES

Yu. I. Bokhovkina

The electroconductivity, viscosity and density of binary systems, formed by acetamide with acetic acid and its chloro derivatives, were investigated in previous studies [1-3]. It was shown that the introduction of chlorine into the acetic acid radical, leads to a substantial increase in the degree of chemical reactivity with acetamide. This found expression in an enhancement of the breaks on the curves of the studied properties in measure with increase in the number of chlorine atoms in the acetic acid radical.

It was natural to expect that the surface tension should also indicate enchancement of chemical reactivity between acetamide and acetic acid and its chloro derivatives in measure with increase in the number of chlorine atoms in the latter. For this reason, we studied the surface tension in the binary systems acetamide-acetic acid, acetamide-monochloroacetic acid and acetamide-trichloroacetic acid.

The method of the highest pressure of a gas bubble was used to study the surface tension [4]. A closed type of vessel was used for the studies. Mercury was used as the seal liquid between the cover, having the capillary tip, and the vessel. A screw arrangement was used for immersion of the capillary tip. The pressure was read on a manometer filled with toluene. To maintain a given temperature (±0.1°), the vessel was placed in a water thermostat. The calculation method has been discussed in detail earlier [5]. The surface tension was expressed in dynes/cm, and the concentration in mole %.

The starting substances were purified before use: acetamide by recrystallization from ether, acetic acid by freezing, and the monochloroacetic and trichloroacetic acids by a double distillation. Their melting points agreed with the tabulated data of [6].

System Acetamide-Acetic Acid

The presence of a 1 : 1 compound with a concealed maximum was established in this system by the fusibility method. The acetic acid branch shows a steep descent to the eutectic at 28.5% acetamide and −17°. Then from the eutectic steeply at first, and then slowly, rises the branch of the compound intersecting the acetamide branch at 48.5% acetamide and −2.4° [7]. The surface tension was studied at 20, 60 and 80° up to 60% acetamide. The surface tension curves, constructed on the basis of the experimental data (Table 1), are shown in Fig. 1 (together with the fusibility diagram). The surface tension shows almost linear change, it strongly increases with increase in the acetamide concentration.

System Acetamide-Monochloroacetic Acid

The presence of two compounds in the system was revealed by the thermal method: the first corresponds to a component ratio of 1 : 1 (distinct maximum at 8°), and the second to the formula $CH_3CONH_2 \cdot 2CH_2ClCOOH$ (concealed maximum). Two eutectic points were found – one at 55.1% acetamide and 5.6°, and the other at 45% acetamide and 4.7°. The peritectic point corresponds to 34.05% acetamide and 13.2° [7].

TABLE 1

Surface Tension in the Binary System of Acetamide Acetic Acid

Mole % CH_3CONH_2	Surface Tension		
	20°	60°	80°
10	29.45	25.38	24.44
15	30.04	26.46	25.03
20	30.83	27.14	25.90
25	31.81	28.02	26.86
30	32.69	28.81	27.64
35	33.57	29.89	28.52
40	34.36	30.69	29.68
45	35.04	31.46	30.47
50	35.93	32.34	31.31
55	—	33.22	—
60	—	33.81	32.88
70	—	—	34.63

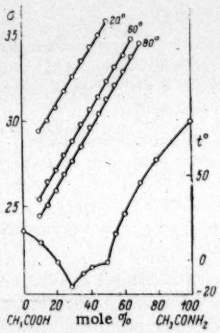

Fig. 1. Surface tension isotherms and fusibility diagram of the system $CH_3COOH-CH_3CONH_2$.

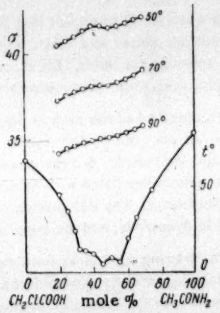

Fig. 2. Surface tension isotherms and fusibility diagram of the system $CH_2ClCOOH-CH_3CONH_2$.

The surface tension was studied at 50, 70 and 90° from 20 to 70% acetamide.

The surface tension isotherms, constructed on the basis of the experimental data (Table 2), are shown in Fig. 2 (together with the fusibility diagram).

The surface tension curves at 50° have a slight maximum at 40% acetamide, which corresponds to the compound of composition $CH_3CONH_2 \cdot 2CH_2ClCOOH$. With elevation of the temperature this maximum is greatly reduced and at 90° only a slight bend is observed instead of a maximum.

TABLE 2

Surface Tension in the Binary System Acetamide-Monochloroacetic Acid

Mole % CH_3CONH_2	Surface Tension		
	50°	70°	90°
20	40.51	37.31	34.15
25	40.80	37.59	34.45
30	41.09	37.81	34.65
35	41.39	38.00	34.81
40	41.72	38.19	34.97
45	41.70	38.20	35.07
50	41.61	38.22	35.15
55	41.72	38.35	35.15
60	41.88	38.59	35.40
65	42.05	38.80	35.61
70	42.25	39.11	35.89

TABLE 3

Surface Tension in the Binary System Acetamide-Trichloroacetic Acid

Mole % CH_3CONH_2	Surface Tension		
	50°	60°	70°
10	—	32.25	31.55
15	—	32.81	32.14
20	34.31	33.42	32.75
25	35.02	34.10	33.46
28	35.51	34.63	33.89
30	35.71	34.92	34.10
35	36.40	35.64	34.84
38	36.81	36.05	35.09
40	37.04	36.27	35.31
45	37.23	36.51	36.79
50	37.57	36.64	36.05
55	37.82	37.05	36.32
60	38.24	37.43	36.53
62	38.87	37.21	36.74
68	38.90	38.12	37.13
70	39.15	38.28	37.36

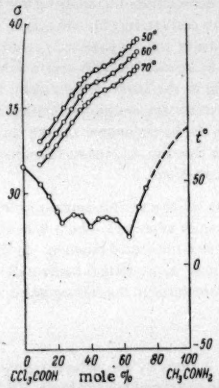

Fig. 3. Surface tension isotherms and fusibility diagram of the system CCl_3COOH–CH_3CONH_2.

System Acetamide-Trichloroacetic Acid

Based on the fusibility, two chemical compositions are revealed in the system:

$CH_3CONH_2 \cdot CCl_3COOH$ and $CH_3CONH_2 \cdot 2Cl_3COOH$,

both of which show distinct maxima (at 26 and 29.3°) and three eutectic points – at 64.12% acetamide and 14.0°, at 41.7% acetamide and 20.6°, and at 24.2% acetamide and 22.3° [7].

The surface tension was studied at 50, 60 and 70° from 10 to 70% acetamide. The surface tension isotherms, constructed on the basis of the experimental data (Table 3), are shown in Fig. 3. The surface tension increases with increase in the amount of acetamide in the mixtures and passes through a maximum corresponding to the composition

$$CH_3CONH_2 \cdot 2CCl_3COOH.$$

With increase in the temperature, the maximum becomes more even and is shifted somewhat toward the acetamide side, which shows a greater surface tension than does trichloroacetic acid.

DISCUSSION OF RESULTS

In the system acetamide-acetic acid, the surface tension at 20, 60 and 80° shows nearly linear change and fails to give any indications of the existence of compounds in the molten homogeneous medium. Apparently the compound $CH_3CONH_2 \cdot CH_3COOH$, strongly dissociated at the melting point, is completely dissociated in the liquid phase.

It is known [8] that the introduction of chlorine in the acetic acid radical increases its acidity, which leads to enhanced chemical reactivity of amides with the chloro derivatives of acetic acid. This circumstance was clearly demonstrated in studying the surface tension of the binary systems formed by urea with acetic acid and its chloro derivatives [5], and also in studying their electroconductivity [9], viscosity and density [10]. This situation was also emphasized in studying the electroconductivity, viscosity and density of the binary systems formed by acetamide with acetic acid and its chloro derivatives [1-3]. A comparison of the surface tension isotherms in the latter systems again leads to the same conclusion. The curves of the surface tension isotherms in the system acetamide-monochloroacetic acid form one slight maximum, which we associate with the existence in the homogeneous molten medium of compounds corresponding to the formula $CH_3CONH_2 \cdot 2CH_2ClCOOH$. The fact that this maximum becomes smoother with elevation of the temperature, indicates strong dissociation of this compound.

The surface tension isotherms in the system acetamide-trichloroacetic acid also possess one maximum, but more sharply expressed, which indicates that a more stable compound of composition $CH_3CONH_2 \cdot 2CCl_3COOH$ is formed in the liquid medium. In this system, with elevation of the temperature, the maximum becomes less smooth than in the system acetamide-monochloroacetic acid, which is associated with the existence of a more stable compound in the homogeneous molten medium.

SUMMARY

1. A study of the surface tension was made in the systems acetamide-acetic acid, acetamide-monochloroacetic and acetamide-trichloroacetic acid.

2. The surface tension isotherms in the system acetamide-acetic acid fail to give any indications of the existence of definite chemical compounds in the homogeneous molten medium.

3. The surface tension isotherms in the systems acetamide-monochloroacetic acid and acetamide-trichloroacetic acid each show a single maximum, which is associated with the presence in the homogeneous medium of the compounds: for the first system $CH_3CONH_2 \cdot 2CH_2ClCOOH$, and for the second system $CH_3CONH_2 \cdot 2CCl_3COOH$.

4. The introduction of chlorine into the acetic acid radical increases its acidity and facilitates the reaction of acetamide with the chloro derivatives of acetic acid.

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THE VISCOSITY OF BINARY SYSTEMS WITH CHLORAL. II

V. V. Udovenko and R. I. Khomenko

Many authors have studied the reaction of chloral with aliphatic alcohols by physicochemical analysis methods [1-7]. In all cases, the presence of sharply expressed chemical interaction was shown, receiving corresponding reflection on the physicochemical diagrams. The aromatic and cyclic alcohols react in the same manner as the aliphatic alcohols [8]. In this paper, we discuss the reaction of chloral with phenols.

The literature contains a large number of studies in which the condensation of chloral with phenols in the presence of various catalysts was investigated [9-15]. No one has studied the reaction of chloral with phenols under ordinary conditions and in the absence of catalysts.

The measurement of the viscosity and density of the systems with phenols, and also the preparation of pure chloral, were done the same as was described in our first communication [8]. The phenol, o-, m-, and p-cresols were purified by repeated distillation. The substances taken for our study had the following boiling points: o-cresol 188.8° (730 mm), m-cresol 198.0° (726 mm), p-cresol 197.0° (730 mm), phenol 178.0° (723 mm), and chloral 96.7° (726 mm).

The viscosity and density values of the pure components are given in Table 1.

The preliminary measurements revealed that the viscosity of the mixtures in the system chloral-phenol changes with time, and becomes constant only after five days; consequently, all of the mixtures after preparation, were sealed in ampuls and held at the boiling point of water for one week. The viscosity measurements were made at 40, 60 and 80°.

The viscosity isotherms of the system chloral-phenol possess an irrational maximum, passing through 25 mole % chloral, which corresponds to the compound $CCl_3CHO \cdot 3C_6H_5OH$ (Fig. 1). With elevation of the temperature, the viscosity maximum becomes flatter and shifts toward the phenol side.

Crystals separate from the mixtures on long standing, which are insoluble in benzene, carbon tetrachloride, chloroform and water, but soluble in alcohol and acetone. After recrystallization from a mixture of alcohol and ether they melted at 203°.

Found %: C 53.06, 52.78; H 3.69, 3.70; Cl 33.31, 33.35. $CCl_3CH(C_6H_4OH)_2$. Calculated%: C 52.91; H 3.46; Cl 33.50.

This compound had been obtained earlier by Meer [16] in the presence of sulfuric and acetic acids as catalysts. Its mixed melting point with the compound synthesized by the Meer method was not depressed.

It was established that the crystals of the compound, obtained by recrystallization from a mixture of alcohol and benzene, effloresce when kept in the air. Their solution in water, containing alkali, leads to the appearance of a layer of benzene on the surface of the solution. To determine the amount of benzene in the crystals of the compound, a sample of the freshly recrystallized substance was placed in a drying oven at 110-120° and kept there until the weight was constant.

Found %: C_6H_6 20.06, 20.14. $C_{14}H_{11}O_2Cl_3 \cdot C_6H_6$. Calculated %: C_6H_6 19.72.

Cases where the substance crystallizes together with benzene are already known in the literature [17].

Substance	Viscosity						Density						
	25°	40°	50°	60°	75°	80°	25°	40°	50°	60°	75°	80°
Chloral	1.0552	0.8503	0.7641	0.7010	0.5885	0.5655	1.5013	1.4766	1.4603	1.4413	1.4186	1.4096
Phenol	—	4.6720	—	2.5260	—	1.5711	—	1.0590	—	1.0428	—	1.0242
o-Cresol	7.3724	—	2.8368	—	1.5210	—	1.0430	—	1.0203	—	0.9995	—
m-Cresol	13.095	—	4.1967	—	2.0118	—	1.0334	—	1.0139	—	0.9951	—
p-Cresol	14.080	—	4.4766	—	2.1135	—	1.0308	—	1.0126	—	0.9923	—

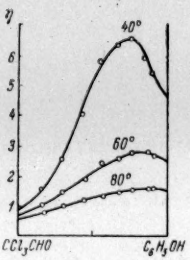


Fig. 1. Viscosity of the system chloral – phenol at 40, 60 and 80°.

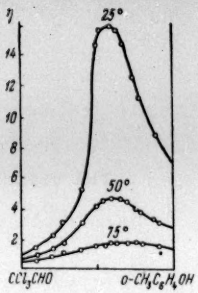


Fig. 2. Viscosity of the system chloral – o-cresol at 25, 50 and 75°.

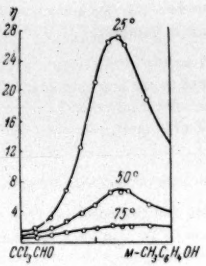


Fig. 3. Viscosity of the system chloral – m-cresol at 25, 50 and 75°.

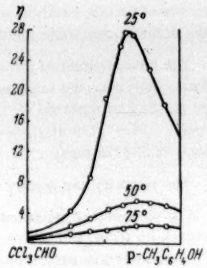


Fig. 4. Viscosity of the system chloral – p-cresol at 25, 50 and 75°.

In the system chloral-o-cresol the viscosity of the mixtures was measured after they had been kept at room temperature for two days. The viscosities of this and the following systems were measured at 25, 50 and 75°. The viscosity isotherms of the system chloral-o-cresol (Fig. 2) pass through an irrational maximum, not corresponding to a rational ratio of the components. With elevation of the temperature the viscosity maximum becomes flatter and shifts toward the o-cresol side.

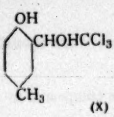
In the system chloral-m-cresol the measurements were made after the mixtures had been kept at room temperature for 4 days. The viscosity isotherms have an irrational maximum (Fig. 3), passing through 33 mole % chloral. With elevation of the temperature the viscosity maximum becomes flatter and is shifted only slightly toward the m-cresol side.

In the system chloral-p-cresol the viscosities were measured after the mixtures had been heated on the water bath for 2 days. The viscosity isotherm at 25° (Fig. 4) represents a curve with a sharply expressed irrational maximum, passing through 33 mole % chloral. With elevation of the temperature the maximum on the isotherms becomes very flat and is shifted toward the p-cresol side.

Crystals of a compound, readily soluble in alcohol, ether, acetone and hot benzene, less readily soluble in cold benzene and carbon tetrachloride, and insoluble in water, are deposited when mixtures of chloral with p-cresol are stored. The compound is obtained as colorless crystals with m. p. 147° when recrystallized from benzene.

Found %: C 42.33, 42.85; H 3.70, 3.68; Cl 41.37, 41.9. $CH_3C_6H_4OH \cdot CCl_3CHO$. Calculated %: C 42.28; H32.52; Cl41.68.

A compound of the same composition with m. p. 147.5° was obtained by Balfe and Webber [15], who studied the reaction of chloral with p-cresol in the presence of hydrogen chloride. They assign structure (X) to it:



(X)

From a comparison of the viscosity diagrams of the systems studied by us, it can be concluded that chloral reacts with both phenol and the cresols. In the systems chloral–phenol and chloral – o-cresol, there occurs the separation of crystalline compounds from the mixtures, the compositions of which fail to agree with the maximum on the viscosity isotherms. Such lack of agreement between the composition of the crystallizing compound and the position of the maximum on the viscosity isotherms is explained by the fact that there are two consecutive processes in these systems. This can be seen on the example of the system chloral-phenol. When chloral is mixed with phenol, a compound is formed at first, in which 1 mole of chloral is combined with 3 moles of phenol. This compound exists only in the liquid phase; the sharp increase in the viscosity of the system is explained by its formation. Such a mixture can be kept for a long time without the separation of any crystals. Chloral can decompose under the influence of light with the liberation of hydrogen chloride [18]. According to our determinations, the latter was formed in the sealed ampuls in an amount of about 0.3 %. Functioning as a catalyst, the hydrogen chloride converts the compound, formed earlier in the liquid phase, into the final product – dihydroxyphenyltrichloroethane, which separates as crystals in measure with its formation.

To verify the expressed considerations, a mixture of chloral with phenol in the mole ratio of 1 : 2 was prepared and kept in sealed ampuls on the water bath for 6 days. Then, one portion of this mixture was methylated, while another portion was acetylated. In the first case, anisole was obtained in 75% yield, while in the second case, phenyl acetate was obtained in 80% yield. Consequently, the addition of chloral to phenol yields not the dihydroxyphenyltrichloroethane, but instead a molecular type of compound due to hydrogen bonding.

The above is also supported by the fact that we obtained the dihydroxyphenyltrichloroethane by the Lunyak method [19]. As our experiments revealed, the formation of the dihydroxyphenyltrichloroethane in benzene solution fails to occur even after a 3-month heating of a mixture of chloral with phenol on the water bath, although, in this case also, the chloral reacts with phenol, forming compounds of the molecular type. However, after passing hydrogen chloride gas into the mixture, crystals of the compound were formed on the third day. From this, it can be assumed that in benzene solution chloral does not decompose under the influence of light and hydrogen chloride is not liberated.

A similar situation exists in the system chloral-p-cresol. But the systems composed of chloral and o- and m-cresols are quite different from the two previous systems. Here crystalline compounds are not formed, and consequently, it can be concluded, in agreement with literature data [15], that under the conditions of our experiments, the condensation of chloral with o- and m-cresol is not evoked by hydrogen chloride.

The systems studied by us are interesting in still another respect. If, for example, the viscosity of a mixture of chloral with phenol is measured at some definite temperature, then completely constant numerical values of the viscosity are obtained. If the given mixture is cooled, and then reheated to the same temperature as before, the numerical values of the viscosity prove to be higher than the values previously obtained. However, if this system is kept at a constant temperature for a longer time than is necessary to reheat the mixture, then the viscosity decreases and gradually approaches the former value. If the mixture is heated above the experimental temperature, with subsequent cooling to the desired temperature, then the viscosity will gradually increase. But the final viscosity values do not remain constant and change somewhat in the direction of increasing. Since the pure components do not possess this property, then this means that a labile equilbrium is established between the components in the mixtures, which equilibrium can slowly shift with change in the temperature.

This property of the examined systems is evidence that the compound of chloral with phenols, formed as the result of hydrogen bonding, is not very stable and dissociates into the components when the temperature is raised. The viscosity isotherms testify to this, the maxima of which bcome flatter with elevation of the temperature and at 75-80° are only weakly expressed.

If the viscosity isotherms of the studied systems are compared among themselves, then it can be seen that the curvature radii of the isotherms at the maximum point are different. In the systems chloral-phenol and chloral-p-cresol they are smaller, while in the systems chloral-o-cresol and chloral-m-cresol, they are greater. From this, it can be assumed that more stable compounds are formed in the first two systems, for which reason they are converted into crystalline products under the influence of hydrogen chloride. This does not occur in the other two systems.

SUMMARY

1. The viscosity of the system chloral-phenol was measured at 40, 60 and 80°, and of the systems chloral-o-cresol, chloral-m-cresol and chloral-p-cresol at 25, 50 and 75°.

2. It was established that chloral, when reacted with phenol, o-, m-, and p-cresol, forms compounds in the liquid phase, which dissociate into the components when the temperature is raised.

3. The compounds of chloral with phenol, o-, m- and p-cresol, formed as the result of hydrogen bonding, do not possess the polyacetal structure.

4. Dihydroxyphenyltrichloroethane separates in the system chloral-phenol, being formed under the influence of a small amount of hydrogen chloride.

5. Trichlorohydroxyethyl-p-cresol separates in the system chloral-p-cresol, being formed in the mixture under the influence of a small amount of hydrogen chloride.

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PHYSICOCHEMICAL STUDY OF THE REACTION OF TITANIUM TETRACHLORIDE WITH THE ESTERS OF MONOBASIC ACIDS

VIII. REACTION OF TITANIUM TETRACHLORIDE WITH n-BUTYL FORMATE AND ISOAMYL FORMATE

Yu. A. Lysenko

It was established in previous studies [1, 2] that titanium tetrachloride reacts with esters of acetic acid to form compounds of the composition $TiCl_4 \cdot E$ and $TiCl_4 \cdot 2E$ (where E is the ester molecule), in which connection compounds of the second type prove to be the less heat stable.

A study of the viscosity, density and conductance of the system titanium tetrachloride-ethyl formate [3] permitted making the conclusion that the components of the given system form the compound $TiCl_4 \cdot 2HCOOC_2H_5$ which is noted for its substantial conductance. To elucidate the influence of the alcohol radical in formic acid esters on their reaction with titanium tetrachloride, we studied the systems titanium tetrachloride-n-butyl formate and titanium tetrachloride-isoamyl formate. Here we determined the viscosity, density and conductance for the indicated systems, and in addition, we investigated the index of refraction for the system titanium tetrachloride-n-butyl formate.

The method used to measure the indicated properties was described earlier [4].

EXPERIMENTAL

System Titanium Tetrachloride-n-Butyl Formate. For the studies we took c. p. titanium tetrachloride, not requiring additional purification. The n-butyl formate was synthesized from c. p. formic acid and butyl alcohol. After long drying over calcium chloride, the ester was fractionally distilled. In our work, we used the fraction with b. p. 106.2–107°; d_4^{20} 0.8908, n_D^{20} 1.3894.

The viscosity, density and conductance were measured at 35, 40, 50, 60 and 70°.

Although the indicated temperature interval could have been expanded somewhat, we did not make any measurements above 70° and below 35°, for the reasons that some tarring is observed above 70° and a strong increase in viscosity below 35°.

As follows, from the viscosity measurement results, expressed in centipoises in Fig. 1, the viscosity isotherms pass through a maximum, the sharp character of which is especially evident for the isotherms at 35, 40 and 50°. At 35°, the maximum on the viscosity isotherm corresponds to 53 mole % n-butyl formate, i. e., it nearly corresponds to the composition of a 1 : 1 compound, but with increase in temperature, a shifting of the maximum is observed along the composition axis toward the ester side and at 70° the maximum corresponds to 58.5 mole % n-butyl formate. It should be mentioned that a considerable flattening of the maximum is also observed with increase in the temperature.

When these data are compared with the results of calculating the absolute and relative temperature coefficients of the viscosity (Fig. 1), it can be assumed that a compound having the composition $TiCl_4 \cdot HCOOC_4H_9$ is formed in the system, in which connection it should be mentioned that there is some inflection on the curve of the relative temperature coefficient in the region of 60–70 mole % ester.

The density measurement results are presented in Fig. 2. Here we show only the isotherms at 35 and 70°, since the form of the remaining isotherms fails to differ from those shown. A substantial deviation from additivity on the density isotherms in the region of 50–70 mole % ester is found to be in accord with the conclusion derived from the viscosity measurement results. The curve of the molecular volumes at 35°, expressed in cm^3/mole of mixture, shows two sharp breaks, corresponding to 53 and 75 mole % n-butyl formate, which is also found to be in accord with the previous conclusion.

The measurements of the index of refraction, taken with an Abbe refractometer for the given system at 35 and 20° (Fig. 3), show that considerable chemical affinity is observed in the system in the region corresponding to an equimolar proportion of the components.

The measurement results obtained by us for the specific conductance are shown in Fig. 4. The conductance isotherms at 35, 40 and 50° each show two well defined minima, corresponding to the composition of the compounds $TiCl_4 \cdot HCOOC_4H_9$ and $TiCl_4 \cdot 2HCOOC_4H_9$.

On the 35° isotherm, one minumum corresponds to 53 mole %, and the other to 68.5 mole % n-butyl formate; here with elevation of the temperature, there is observed at 60 and 70°, some shifting of the minima along the composition axis toward the ester side and their becoming smoother, which can be explained by the sharp viscosity decrease in the system, and the dissociation of the formed compounds. The results of calculating the absolute and relative temperature coefficients of the conductance, and also the derived conductance at 35° (Fig. 4), agree with the measurement data obtained for the specific conductance. As a result, on comparing the results of measuring all of the properties for the system titanium tetrachloride-n-butyl formate, it is necessary to conclude that two compounds are formed in the system: $TiCl_4 \cdot HCOOC_4H_9$ and $TiCl_4 \cdot 2HCOOC_4H_9$, which dissociate in the liquid phase.

System Titanium Tetrachloride-Isoamyl Formate. The isoamyl formate used for the study was synthesized from c. p. formic acid and isoamyl alcohol. After drying over calcium chloride and fractional distillation, we took for our study the fraction with b. p. 123.2–123.6°; d_4^{20} 0.8713, n_D^{20} 1.3979.

All of the measurements were made at 50, 60, 70 and 80°. Below 50° the formation of crystals is observed in the solutions with an ester content ranging from 20 to 50 mole %; tarring of the solutions begins at temperatures above 80°.

The viscosity measurement results are presented in Fig. 5.

The maxima on the viscosity isotherms at 50, 60 and 70° correspond to 55 mole % isoamyl formate. At 80° the maximum proves to be shifted somewhat toward the ester side and corresponds to 60.6 mole % isoamyl formate, which permits the conclusion that the compound $TiCl_4 \cdot HCOOC_5H_{11}$, dissociating in the liquid phase, is formed. Calculation of the absolute and relative temperature coefficients of the viscosity leads to the same conclusion (Fig. 5). The curve of the absolute temperature coefficient shows a sharply expressed maximum, corresponding to 55 mole % isoamyl formate. The maximum on the curve of the relative temperature coefficient of the viscosity corresponds to the same composition. It should be mentioned that, the same as for the system titanium tetrachloride-n-butyl formate, the curve of the relative temperature coefficient of the viscosity shows an inflection in the region of 60-70 mole % ester.

The density isotherms, derived for 50 and 80° in Fig. 6, indicate considerable compression, which occurs for the given system in the region of 50–65 mole % isoamyl formate. The deviation from additivity, testifying to considerable chemical affinity between the components, is especially well manifested on the curve of the molecular volumes for 50°, having two sharp breaks corresponding to 50 and 72.5 mole % isoamyl formate.

The clearest reflection of reactivity between titanium tetrachloride and isoamyl formate is found on the specific conductance isotherms (Fig. 7). The conductance isotherm at 50° passes through a minimum, corresponding to 70 mole % isoamyl formate, and shows a sharp inflection, corresponding to 55 mole % of the ester.

With elevation of the temperature, a noticeable straightening out of the minima and a nearly complete evening out of the inflections is observed on the conductance isotherms at 60, 70 and 80°, which, the same as for the previous system, can be explained by the thermal dissociation of the formed compounds of composition $TiCl_4 \cdot HCOOC_5H_{11}$ and $TiCl_4 \cdot 2HCOOC_5H_{11}$. The formation of these compounds finds verification in the form of the curves of the absolute and relative temperature coefficients of the conductance, the calculated values of which are shown in Fig. 7.

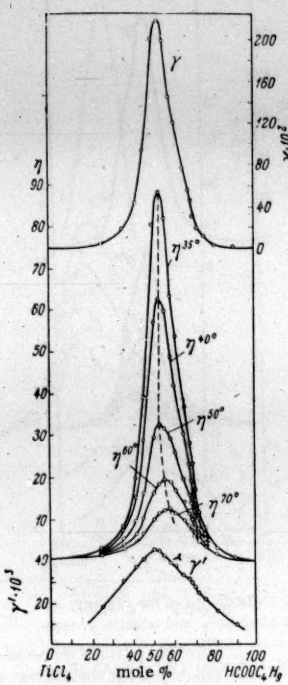

Fig. 1. Viscosity (η) isotherms of the system $TiCl_4$–$HCOOC_4H_9$, and the absolute (γ) and relative (γ') temperature coefficients of the viscosity.

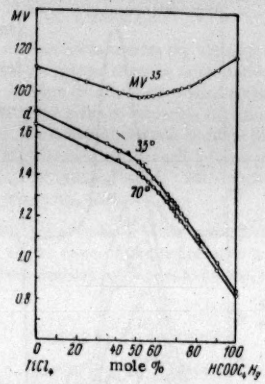

Fig. 2. Density and molecular volume isotherms of the system $TiCl_4$–$HCOOC_4H_9$.

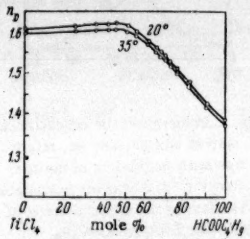

Fig. 3. Index of refraction of the system $TiCl_4$–$HCOOC_4H_9$.

The derived conductance curve for 50° passes through a maximum, nearly corresponding to an equimolar ratio of the components (Fig. 7). The results of studying the viscosity, density and conductance for the system titanium tetrachloride-isoamyl formate permit the conclusion that two compounds, $TiCl_4 \cdot HCOOC_5H_{11}$ and $TiCl_4 \cdot 2HCOOC_5H_{11}$, showing dissociation in the liquid phase, are formed in the system.

As follows from the data obtained by us, the reaction of titanium tetrachloride with the esters of formic acid leads to the formation of compounds with the composition $TiCl_4 \cdot E$ and $TiCl_4 \cdot 2E$, in which connection, an increase in the size of the alcohol radical exerts little influence on the stability of compounds of the second type. A study that we had made earlier [2, 4] of the reaction of titanium tetrachloride with n-propyl acetate, n-butyl acetate and isoamyl acetate reveals than an increase in the size of the alcohol radical exerts substantial influence on the stability of compounds of the type of $TiCl_4 \cdot 2E$ in the case of acetates, and in going to the radical C_5H_{11} the compound $TiCl_4 \cdot 2CH_3COOC_5H_{11}$ proves to be nearly completely dissociated at 60-70°. A comparison of the results of studying the reaction between titanium tetrachloride and the esters of formic acid with the data on the reaction between titanium tetrachloride and the esters of acetic acid leads to the conclusion that compounds of the type of $TiCl_4 \cdot 2E$ are somewhat more stable in the case of the formates.

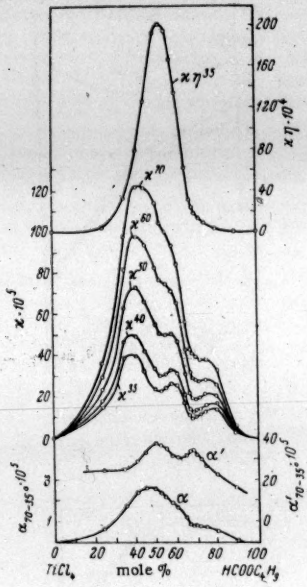

Fig. 4. Isotherms of the conductance κ, derived conductance $\kappa\eta$, relative temperature coefficient of the conductance α', and absolute temperature coefficient of the conductance α of the system $TiCl_4$–$HCOOC_4H_9$.

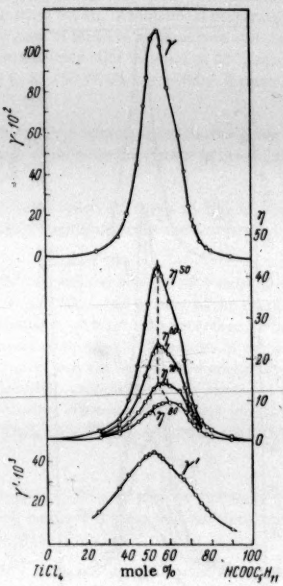

Fig. 5. Isotherms of the viscosity η, and absolute γ and relative γ' temperature coefficients of the viscosity γ of the system $TiCl_4$–$HCOOC_5H_{11}$.

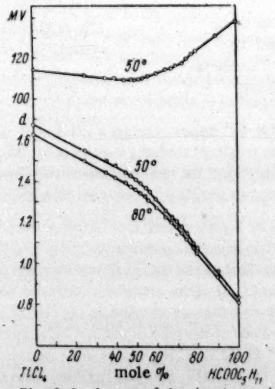

Fig. 6. Isotherms of the density and molecular volume of the system $TiCl_4$–$HCOOC_5H_{11}$.

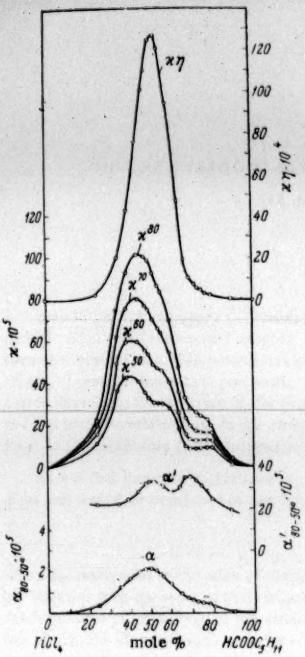

Fig. 7. Isotherms of the conductance χ, derived conductance $\chi\eta$, and relative α' and absolute α temperature coefficients of the conductance of the system $TiCl_4$–$HCOOC_5H_{11}$.

SUMMARY

1. On the basis of measuring the viscosity, density and conductance of the systems titanium tetrachloride-isoamyl formate and titanium tetrachloride-n-butyl formate (a supplementary study of the index of refraction was also made for the latter system), it was established that titanium tetrachloride reacts with n-butyl formate and isoamyl formate to give the compounds: $TiCl_4 \cdot HCOOC_4H_9$, $TiCl_4 \cdot 2HCOOC_4H_9$, $TiCl_4 \cdot HCOOC_5H_{11}$ and $TiCl_4 \cdot 2HCOOC_5H_{11}$.

The stability of compounds of the type of $TiCl_4 \cdot 2E$ is somewhat greater for the esters of formic acid than it is for similar compounds from titanium tetrachloride and the esters of acetic acid.

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ON THE PERIODIC RELATIONSHIP OF ELECTRODE POTENTIALS OF METALS IN FUSED SALTS

Yu. K. Delimarsky

Even in 1913, L. Chugaev [1] postulated that the so-called normal electrode potentials should change as a periodic function of the atomic weights. H. S. Taylor [2] later indicated that a periodic relationship exists between the normal electrode potentials (in water solutions) and the atomic numbers. At the present time, it is known [3] that the ionization potentials, and also the work values for the escape of electrons, which to some degree depend on the structure of the external electron layers of the atoms of corresponding elements, are found to be in periodic relationship to the atomic numbers. Evidently, the external electron cloud of an atom also plays an important role in the formation of the electrode potential.

As was first shown by L. Pisarzhevsky [4], the magnitude of the electrode potential of a metal in a solution of its ions should be composed of two terms:

$$E = E_0 + \Delta E, \qquad (1)$$

where E_0 corresponds to the work of cleaving the electrons and is independent of the nature of the solvent, and ΔE corresponds to the work of ionic migration from the electrode into solution. The second term determines the magnitude of the energy of solvation of ions and depends chiefly on the properties of the solvent. As a result of this, the electrochemical series of metals can be different in different solvents. However, evidently, the main component of the electrode potential is the work of electron escape; consequently, independent of the solvent, the electrode potential values of metals should be found in periodic relationship to their order numbers. The relationship between the normal electrode potentials (in water solutions) and the atomic numbers is shown in Fig. 1. The same relationship for acetonitrile solutions is shown in Fig. 2. The values of the electrode potentials in acetonitrile were taken from the study of V. Pleskov [5]. As can be seen from Figs. 1 and 2, all of these

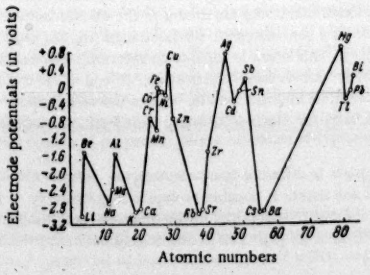

Fig. 1. Normal electrode potentials in water solutions.

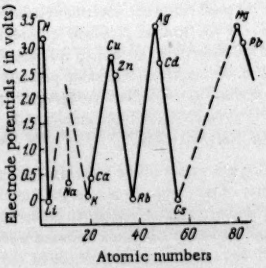

Fig. 2. Electrode potentials of metals in acetonitrile solutions.

relationships show a well defined periodic character.

It seemed of interest to us to determine if the electrode potentials in fused salts, the treatment of which is inconvenient if the theories of L. V. Pisarzhevsky are used, obey some sort of rule. First, as a rule, solvation is absent in fused salts, and second, the opinions of L. V. Pisarzhevsky, relative to the origin of the electrode potential, are somewhat antiquated. At the present time, the electrode potential is regarded as being a value that is composed of not less than four jumps of the potential (at the four phase boundaries): metal I (m_I)–solution I (s_I), metal II (m_{II})–solution II (s_{II}), metal I–metal II, solution I–solution II.

$$E = E_1 - E_2 = V_{m_I s_I} + V_{s_I s_{II}} + V_{s_{II} m_{II}} + V_{m_I m_{II}}, \qquad (2)$$

where: E_1 and E_2 are the electrode potentials, E is the emf of the galvanic element, and $V_{m_I s_I}$, $V_{s_I s_{II}}$, etc., are the corresponding jumps of the potential at all of the phase boundaries of the galvanic element.

In fused salts, the jump in potential at the boundary of solution I–solution II (diffusion potential) is small, since at elevated temperatures the diffusion coefficients of different ions do not differ greatly between themselves. Consequently, as a first approximation of the term ($V_{s_I s_{II}} = 0$) can be neglected in the jump of the potential at the boundary, of solution I-solution II. The jump in potential at the boundary of metal I-metal II depends on the differences in the work of electron escape from the two metals. If all of the electrode potentials are compared with reference to the same metal, then the relative magnitude of this jump will be determined by the work of electron escape for the metal whose electrode potential is under consideration. One of the jumps in the potential of metal-solution is assumed to be constant ($V_{m_{II} s_{II}} = \text{const}$), and then E_2 is conditionally taken equal to zero. Consequently:

$$E = E_1 = V_{m_I s_I} + V_{m_I m_{II}} + \text{const}, \qquad (3)$$

where m_I is the metal whose electrode potential is being determined. The values $V_{m_I m_{II}}$, depending on the work of electron escape, should be a periodic function of the atomic numbers. The value $V_{m_I s_I}$ is associated with the energy change that occurs when a metal ion migrates from the crystal lattice of the metal into the molten electrolyte. As yet, we have very little information relative to the magnitude of this energy and the possibility of calculating it. If it is assumed that this value depends on the chemical properties of the metal ions, then this component of the electrode potential should also be considered as being a periodic function of the atomic numbers. As a result, it should be expected that the electrode potentials of metals in fused salts will change as a periodic function of the atomic numbers. To verify this statement, we constructed graphs with the coordinates: electrode potentials of metals in fused salts/atomic numbers. However, the values of the electrode potentials in fused salts lacked the precision that prevails in this respect for aqueous solutions.

The generally accepted zero electrode (similar to the hydrogen electrode for aqueous solutions) and the reversible standard reference electrode (similar to the calomel electrode) are absent in the electrochemistry of fused salts. At the time we proposed the sodium electrode as a zero electrode for fused salts [6], and later we developed the reversible tin-sodium reference electrode [7]. This made it possible to determine and calculate the values of the individual electrode potentials of metals in various fused electrolytes. In one of our earlier published studies [8] we derived the specific electrode potentials of some metals, both in individual fused halides and in some more complex fused electrolytes, and specifically in: NaCl–KCl–$SrCl_2$; NaCl–$AlCl_3$; NaBr–KBr; NaBr–$AlBr_3$; NaI; NaI – AlI_3.

Knowing the values of the individual electrode potentials in different fused electrolytes permits elucidating the character of their dependence on the atomic numbers and makes it possible to depict it graphically on the coordinate scale: values of electrode potentials–atomic numbers. The values of the electrode potentials in fused sodium fluoride were taken from the study of F. F. Grigorenko [9]. The corresponding data are presented in Figs. 3–6 and relate to a temperature of 700°.

From the derived graphs, it can be seen that despite the great difference between the values of the electrode potentials in different fused electrolytes (and also a difference in the electrochemical series), the general character of the curves is the same for all of the electrolytes.

At the maximum points (or close to them) on nearly all of the diagrams, are found beryllium, aluminum, cobalt (or nickel), copper, silver, antimony, mercury and bismuth. Correspondingly, the alkali and alkaline-earth metals, and also thallium, are usually found at the minimum points. Such an arrangement of the metals on the basis of their electrode potential values is retained in both individual fused salts and fused salt mixtures, taken as the electrolytes [10].

It is interesting to mention that the mutual distribution of the metals on all of the graphs, respectively relating to the fused chlorides, bromides and iodides, is completely the same, and coincides with the situation that we see in Fig. 1 for aqueous solutions. Some difference is observed for the fused fluorides.

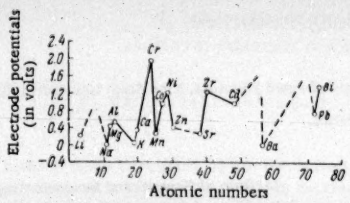

Fig. 3. Electrode potentials of metals in fused fluorides.

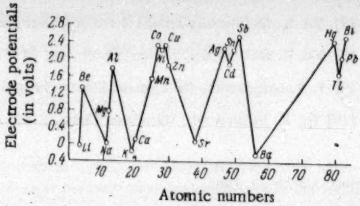

Fig. 4. Electrode potentials of metals in fused chlorides.

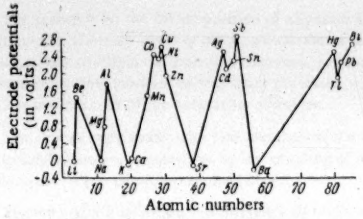

Fig. 5. Electrode potentials of metals in fused bromides.

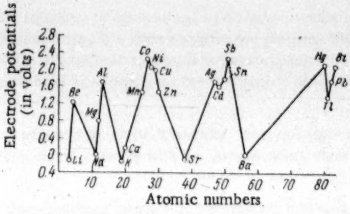

Fig. 6. Electrode potentials of metals in fused iodides.

These facts are evidence that the electrode potentials of metals, independent of the solvent, are first of all a function of the fundamental properties of chemical elements, determined by their position in the D. I. Mendeleev periodic system. The other factors, like temperature, solvent and nature of the anion, can influence both the values of the electrode potentials and the mutual distribution (order) of the metals in the electrochemical series of voltages. However, these supplementary factors do not change the general character of the relationship (in the given case a periodic relationship) between the values of the electrode potentials and the fundamental chemical properties of the elements as represented by their Mendeleev numbers.

SUMMARY

1. Graphs were constructed with the coordinates: value of the metal electrode potential (in various fused electrolytes) – atomic number. The values of the individual electrode potentials were taken relative to the electrode potential of sodium, the value of which was conditionally taken as equal to zero.

2. It was shown that in various fused electrolytes, the electrode potential values of metals are a periodic function of their order numbers, in which connection the same mutual distribution of the metals is retained, independent of the nature of the fused salts in which the electrode potentials are determined.

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REACTION OF FREE RADICALS IN SOLUTIONS

VI. MECHANISM OF THE DECOMPOSITION OF ALIPHATIC AROMATIC TRIAZENES IN THE PRESENCE OF WATER AND ACIDS

V. Ya. Andakushkin, B. A. Dolgoplosk and I. I. Radchenko

Recently it was established [1] that the thermal decomposition of aliphatic aromatic diazoamino compounds (triazenes) in hydrocarbon media, in the absence of water proceeds monomolecularly with the formation of aryl and alkyl free radicals in accord with the scheme:

$$ArNH{-}N{=}N{-}R \longrightarrow ArNH\cdot + N_2 + R\cdot$$

The reaction for the decomposition of aliphatic aromatic triazenes in aqueous and hydrocarbon media under the influence of either water or acids, as was shown in the present study, is a more complicated process. The decomposition of aliphatic aromatic triazenes, in contrast to the aromatic triazenes, is not accompanied by the noticeable development of secondary processes, which permitted us to elucidate the mechanism of the main reaction and the role of the activating additives.

The studies were made with two members of the class of aliphatic aromatic triazenes: methylphenyl- and butylphenyltriazenes, synthesized by the coupling of phenyldiazonium chloride with the corresponding monoalkylamines by the Dimroth method [2].

Figures 1 and 2 illustrate the influence of water on the decomposition kinetics of methylphenyltriazene and butylphenyltriazene in methyl alcohol.

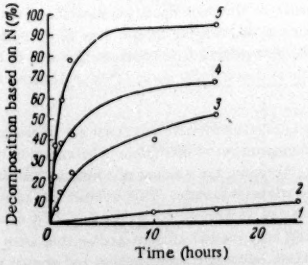

Fig. 1. Decomposition of methylphenyltriazene in aqueous methyl alcohol solutions at 20°. Concentration of alcohol (in volume %): 1) 99.0, 2) 95.0, 3) 75.0, 4) 50.0, 5) 25.0.

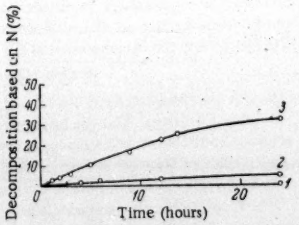

Fig. 2. Decomposition of butylphenyltriazene in aqueous methyl alcohol solutions at 20°. Concentration of alcohol (in %): 1) 99, 2) 95, 3) 80.

The triazenes failed to decompose in anhydrous alcohol at room temperature. Dilution of the alcohol with water resulted in uniform increase in the decomposition rate. Similar results were obtained when the aliphatic aromatic triazenes were decomposed in water-hydrocarbon mixtures (Figs. 3 and 4).

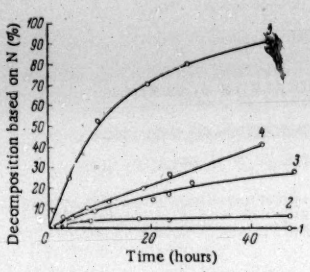

Fig. 3. Decomposition of methylphenyltriazene in hydrocarbon-water mixtures at 20°.
1) dry benzene, 2) moist benzene, 3) benzene-water mixture, 4) benzene emulsion, 5) water.

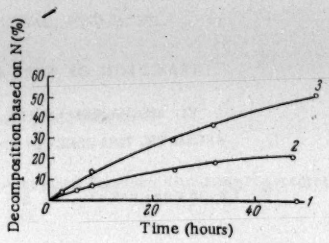

Fig. 4. Decomposition of butylphenyltriazene in hydrocarbon-water mixtures at 20°.
1) dry benzene, 2) benzene emulsion, 3) water.

In benzene and isopropylbenzene, dried over metallic sodium, the triazenes do not decompose at 20 and 40°. In the same hydrocarbons, without special drying, there occurred very slow decomposition, reaching a depth of 10–12% in 100–110 hours. When the hydrocarbon, containing the triazene with water, was shaken continuously, the decomposition proceeded with noticeable speed even at room temperature, reaching a depth of 23–25% in 48 hours. The introduction of an emulsifier (sodium salt of di-sec-butylnaphthalenesulfonic acid) into these systems, increasing the surface of separation between the water and hydrocarbon phases, resulted in increasing the decomposition rate by approximately 1.5 times. The methylphenyltriazene was decomposed most rapidly at these temperatures when it was suspended in water. In 48 hours the decomposition had reached a depth of 90%.

The pH of the medium was found to exert a strong influence on the decomposition kinetics of the triazenes in water and in benzene emulsions. • In the pH interval studied by us, ranging from 1.0 to 12.5, the fastest decompostion rate occurred at a pH of 1.0. An increase in the pH retarded the decomposition and in strongly alkaline media (ph > 10.0) the decompostion of the triazenes was exceedingly slow. This is illustrated in Figs. 5 and 6.

Various gaseous and liquid products are formed when the aliphatic aromatic triazenes are decomposed in water and in benzene emulsions. The gas liberated in the decomposition of methylphenyltriazene in water (at 20°) and in neutral emulsions (at 50°) was almost entirely pure nitrogen, the amount of which in all cases corresponded to exactly 2/3 of the total amount of nitrogen in the triazene sample. This amount was taken as the theoretical. In addition to nitrogen, ethane was present in the gas, in amount not exceeding 2.5% of the theoretical. In the condensate, in amounts close to theoretical, only methyl alcohol and aniline were found. Very characteristic was the complete absence of aliphatic amines, aromatic hydrocarbons and phenol in the decomposition products, which indicates the absence of tautomeric transformations, characteristic for the aromatic triazenes, and permits assigning to the triazenes only the structure $C_6H_5NH—N=N—R$.

• The desired pH was obtained by adding the proper amounts of either hydrochloric acid or potassium hydroxide to the system.

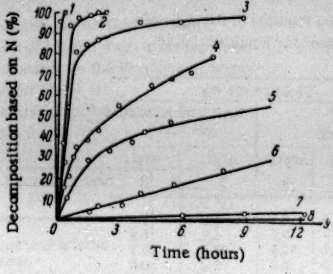

Fig. 5. Influence of the pH of the medium on the decomposition kinetics of methylphenyltriazene in water at 20°.
pH values: 1) 1.0, 2) 2.0, 3) 4.02, 4) 5.13, 5) 6.62, 6) 8.1, 7) 10.96, 8) 11.8, 9) 12.52.

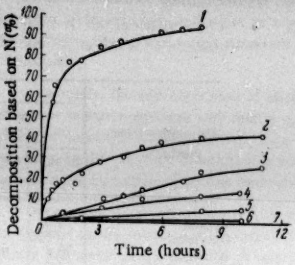

Fig. 6. Influence of the pH of the medium on the decomposition kinetics of butylphenyltriazene in water at 20°.
pH values: 1) 1.0, 2) 3.0, 3) 5.13, 4) 6.88, 5) 8.06, 6) 9.8, 7) 11.0.

In addition to nitrogen, the gas obtained in the decomposition of the butylphenyltriazene contained butane and butylene, in which connection, the amount of butylene proved to be considerably greater than the amount of butane. Only aniline and butanol were found in the condensate. The formation of butane and butylene is associated with a corresponding reduction in the butanol yields.

The analysis results obtained for the decomposition products of the methylphenyltriazene and butylphenyltriazene are shown in Tables 1 and 2.

The volumes of gas liberated in the decomposition of methylphenyltriazene in aqueous hydrochloric acid solutions were always greater than those obtained in neutral media, and uniformly increased in measure with reduction in the pH. When 2.0–2.5N HCl solutions were used, the increase in the volumes of gas, above the theoretical based on the nitrogen, reached 35–45%. It was established by analysis that methyl chloride is present in the gas, the yield of which increased with increase in the hydrochloric acid concentration. The formation of methyl chloride is the result of one of the decomposition acts of the triazene, since hydrochloric acid and methyl alcohol do not react with each other under the indicated conditions.

TABLE 1

Composition of the Decomposition Products of Methylphenyltriazene in Water at 20° and in Benzene Emulsions at 50°

Decomposition products	Yield (mole %)				
	water (pH 7.02)			benzene emulsion (pH 6.93)	
	expt. 1	expt. 2	expt. 3	expt. 1	expt. 2
Methane	0.0	0.0	0.0	0.0	0.0
Ethane	0.0	0.8	2.7	0.0	2.6
Nitrogen	99.2	100.0	99.2	98.8	97.4
Methylamine	0.0	0.0	0.2	0.0	0.0
Methanol	95.0	98.5	100.2	97.5	96.4
Aniline	98.0	94.8	96.7	96.9	95.6
Aromatic hydrocarbons	0.0	0.0	0.0	Not determined	
Phenol	0.3	0.0	0.0	0.0	0.2

TABLE 2

Composition of the Decomposition Products of Butylphenyltriazene in Water at 20° and in Benzene Emulsions at 50°

Decomposition products	Yield (mole %)				
	water (pH 7.02)			benzene emulsion (pH 6.59)	
	expt. 1	expt. 2	expt. 3	expt. 1	expt. 2
Butane	1.33	2.6	4.1	1.9	2.3
Butylene	3.65	3.8	8.5	4.9	6.8
Nitrogen	98.6	98.1	99.8	98.4	99.7
Butylamine	0.0	0.0	0.0	0.0	0.0
Butanol	78.8	86.7	83.2	74.8	87.5
Aniline	98.0	100.0	98.6	91.5	94.8
Aromatic hydrocarbons	0.0	0.0	0.0	Not determined	
Phenol	0.0	0.0	0.0		

As is revealed by the analysis results given in Table 3, the formation of methyl chloride during the decomposition of the triazenes is associated with a reduction in the methanol yields, with retention of quantitative yields of the aniline.

TABLE 3

Composition of the Decomposition Products of Methylphenyltriazene in Aqueous Hydrochloric Acid Solutions at 20°

HCl concentration (M)	Found (mole %)		
	CH_3Cl (based on the gas)	methanol	aniline
0.0	—	97.8	94.8
0.001	0.0	95.6	100.0
0.1	15.0	84.8	95.7
2.0	38.0	57.0	99.8
2.5	46.0	50.2	98.2

TABLE 4

Composition of the Decomposition Products of Methylphenyltriazene in Benzene Under the Influence of Oleic Acid at 20°
(Mole ratio triazene: acid in Expt. 1 = 1 : 1, and in Expt. 2 = 1 : 2)

Decomposition products	Yield (mole %)	
	expt. 1	expt. 2
Methane and ethane	0.0	Not found
Aniline	97.4	100.0
Methylaniline	2.8	0.0
Methanol	7.0	0.0
Free oleic acid (based on acid number)	6.7	50.6
Methyl oleate (based on ester number)	88.6	97.8

TABLE 5

Composition of the Decomposition Products of Methylphenyltriazene in Benzene Under the Influence of Benzoic Acid at 20°.
(Mole ratio triazene : acid = 1 : 1)

Decomposition products	Yield (mole %)
Methanol	0.0
Methyl benzoate (based on ester number)	99.3
Amount of methanol recovered from methyl benzoate	84.2

The decomposition of the aliphatic aromatic triazenes in hydrocarbon media was greatly accelerated in the presence of organic acids (Fig. 7), and was accompanied by the nearly quantitative formation of esters, which is illustrated by the experimental data obtained in the decomposition of methylphenyltriazene in benzene solutions in the presence of oleic and benzoic acids (Tables 4 and 5). These data agree with the results obtained by V. Ya. Pochinok and O. I. Shevchenko [3], who established the possibility of alkylating carboxylic acids and phenol with alkylphenyltriazenes.

TABLE 6

Composition of the Decomposition Products of Methylphenyltriazene in Isopropylbenzene in the Presence of Water and Sulfur at 50°
(Concentration of triazene in isopropylbenzene 0.1M)

Decomposition products	Yield (mole %)
Methane and ethane	0.0
Methanol	64.2
Aniline	103.6
Dimethyl polysulfide	30.0

From the obtained data, it follows that in the mutual presence of organic acid and water in a hydrocarbon medium, the reaction proceeds simultaneously with both components.

As a result, the decomposition of aliphatic aromatic triazenes in water proceeds with nearly quantitative yields of aniline and alcohols, while in a hydrocarbon medium, in the presence of acids, it proceeds with the quantitative formation of aniline and esters.

Decomposition of the aliphatic aromatic triazenes in aqueous media initiates polymerization, which is a direct indication of the presence of intermediate radical stages.

The data presented above on the composition of the decomposition products of triazenes, in particular the formation of butane and butylene with a corresponding reduction in the butanol yields, and also the formation of esters of carboxylic acids, have already indicated that the origin of free radicals is associated with the stages leading to the formation of either alcohol or ester. We obtained experimental support of this conclusion by studying the composition of the products formed in the decomposition of triazenes in the presence of free radical acceptors.

As free radical acceptors, we used sulfur and styrene. As had been established by E. I. Tinyakova and others [4], in the thermal decomposition of triazenes in hydrocarbon media, the formed alkyl radicals are quantitatively trapped by sulfur with the formation of dialkyl polysulfides. The role of styrene, as a free radical acceptor, is associated with the development of polymerization.

We studied the composition of the decomposition products of methylphenyltriazene in aqueous-emulsion medium at 50°. As the hydrocarbon phase, we used a solution of the triazene and sulfur in isopropylbenzene. We took 2.5 g of sulfur for 1 g of triazene. The experimental data are given in Table 6.

A considerable amount of dimethyl polysulfide is formed in the presence of sulfur, with a corresponding reduction in the yield of methanol. These data serve as direct evidence that the origin of free radicals is associated with the stages that precede the formation of the alcohol. Similar results were obtained when we used the methylphenyltriazene in aqueous-emulsion medium to initiate the polymerization of styrene (Table 7).

Participation of the triazene in initiating polymerization is associated with a reduction in the yields of alcohol. In all cases, the aniline is formed in practically quantitative yields.

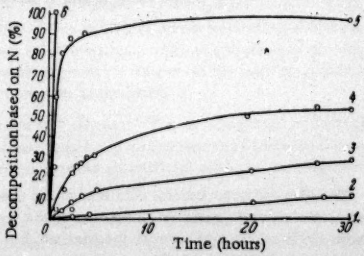

Fig. 7. Influence of oleic acid on the decomposition kinetics of methylphenyltriazene in benzene at 20°.
Mole ratio of acid to triazene: 1) 0.0, 2) 0.1, 3) 0.25, 4) 0.50, 5) 1.0, 6) 2.0.

As a result, on the basis of our work, it was established that the decomposition of aliphatic aromatic triazenes in the presence of water proceeds by a different mechanism than in hydrocarbon media. Water assumes direct chemical participation in the decomposition process, and its elements enter into the composition of the main final products.

On the basis of the experimental data, this mechanism can be depicted as follows:

$$C_6H_5NH-N=N-R + HOH \longrightarrow C_6H_5NH_2 + RN=N-OH.$$

$$\downarrow$$

$$R\cdot + \cdot OH + N_2$$

$$\downarrow$$

$$ROH$$

A reduction in the methanol yield when methylphenyltriazene is decomposed in the presence of either styrene or sulfur, and the formation in the latter case of substantial amounts of dimethyl polysulfide

$$CH_3\cdot + S_8 \longrightarrow CH_3S_n\cdot \longrightarrow CH_3S_mCH_3$$

are direct evidence that the formation of the radicals is associated with the decomposition stage of the alkyldiazohydroxide.

In the decomposition of butylphenyltriazene the liberated gas contained a substantial excess of butylene when compared with butane. This finds explanation in the fact that it was the radicals formed in the decomposition of the alkyldiazohydroxide that were mainly involved in the disproportionation reaction:

$$CH_3CH_2CH_2CH_2\cdot + \cdot OH \longrightarrow H_2O + CH_3CH_2CH=CH_2.$$

The decomposition of methylphenyltriazene in a hydrocarbon medium in the presence of either oleic or benzoic acid gave nitrogen, aniline and the corresponding methyl alcohol esters in quantitative yields, which is in accord with the following scheme:

$$R_1C(=O)-OH + C_6H_5NHN=NR \longrightarrow R_1C(=O)-O-N=NR + C_6H_5NH_2$$

$$\downarrow$$

$$R_1C(=O)-O\cdot + R\cdot + N_2$$

$$\downarrow$$

$$R_1C(=O)-OR$$

The obtained experimental data lead to the conclusion that initiation of polymerization under the influence of aliphatic aromatic triazenes in aqueous media is conditioned by the development of two consecutive processes: 1) the addition of water to the triazene, and 2) the spontaneous decomposition of the alkyldiazohydroxides with the formation of free radicals. The rate at which the water adds determines the general kinetics of the whole process.

The stated considerations are also valid for the decomposition of triazenes in hydrocarbon media in the presence of organic acids.

For the decomposition of triazenes in aqueous hydrochloric acid solution the reaction apparently proceeds by a different path, since this decomposition, leading to the formation of an alkyl chloride, could not be used to initiate polymerization. By analogy with aromatic diazo compounds, it is possible that here the reaction proceeds in the direction of forming a diazonium chloride of structure $R-N\equiv N$ (Cl), the decomposition of which

leads immediately to the final product: $RN{=}N{-}\underset{\underset{Cl}{|}}{}\rightarrow RCl + N_2$.

TABLE 7

Amount of Aniline and Methanol in the Latex

Expt. nos.	Decomposition of the triazene (%)	Degree of polymerization (%)	Found (mole %)	
			methanol	aniline
1	52.1	55.2	71.6	94.7
2	55.0	61.7	70.4	98.9

EXPERIMENTAL

a) Study of the Decomposition Kinetics of Aliphatic Aromatic Triazenes. The decompostion of the triazenes was run in an atmosphere of thoroughly purified nitrogen. The experiments on the decomposition of triazenes in water, alcohol and in hydrocarbons were run in an ampul, connected to a dropping funnel, by means of which the investigated liquids were introduced, and also connected to a gas burette, filled with saturated sodium chloride solution. In the experiments where the triazenes were decomposed in anhydrous media, the burette was filled with mercury.

The decomposition of the triazenes in emulsions was run in an apparatus fitted with a mercury-seal stirrer. The construction of the seal was such that it permitted the use of quite a high vacuum (0.1–0.5 mm), which was necessary for the complete removal of air from the apparatus.

b) Polymerization of Styrene in Emulsions. The following general directions were used to prepare the starting emulsions for polymerization: 100 weight parts of styrene, 0.005 mole of the triazene, 5 wt. parts of emulsifier (Nekal), and 110 wt. parts of water.

The polymerization was run in ampuls at 50°. The hydrocarbon and water phases were charged into the ampuls under conditions that excluded the admittance of air into the system. After polymerization, the ampuls were opened and the extent of triazene decomposition determined from the amount of liberated gas, while the degree of polymerization was determined by the amount of polymer in the latex.

c) Method for the Analysis of the Decomposition Products of Triazenes. The decomposition products of the aliphatic aromatic triazenes were analyzed by various methods, depending on the chemical nature of the substances being determined. The suitability of each method was checked on artificial mixtures, in composition close to those of the real systems.

In the gas obtained in the decomposition of the aliphatic aromatic triazenes, the amount of lower saturated hydrocarbons was determined by combustion over copper oxide (methane and ethane for the case of methylphenyltriazene decomposition, and butane for the case of butylphenyltriazene decomposition). In addition to butane, the amount of butylene in the gas obtained from the decomposition of the butylphenyltriazene was determined by the method of absorption in bromine water. The methyl chloride was determined by the method of burning its mixture with either hydrogen or acetylene in a quartz lamp, connected to a system of absorbers filled with standard silver nitrate solution.

The water and hydrocarbon phases were respectively analyzed for their content of aliphatic amines, alcohols, esters, aromatic amines and phenol. To determine the aliphatic amines, a test sample was made alkaline and then distilled. The distillate was collected in a receiver containing standard hydrochloric acid, the excess of which was later titrated with alkali in the presence of phenolphthalein. The presence of aromatic amines in the distillate failed to influence the determination accuracy, since their salts react as free acids when phenolphthalein is used as indicator [5].

The Fischer-Schmidt method was used to determine the amount of methyl alcohol [6]. The advantage of this method is the fact that the determination accuracy is not influenced by the presence of hydrocarbons, aromatic amines and phenols in the analyzed mixtures.

The butyl alcohol was determined by the Alekseeva method [7], but here the butanol was first separated from the aniline by its extraction with benzene from the acidified sample.

The esters were determined by the ester number method, using alcoholic sodium hydroxide as the saponification agent. In some cases, the formed ester could be saponified with aqueous sodium hydroxide solution. When this was done, the recovered alcohol could be determined quantitatively.

The total amount of aromatic amines was determined by the Kolthoff bromination method [8]. Aniline was determined by the diazotization method, with subsequent coupling of the phenyldiazonium chloride with β-naphthol [9]. The express method [10], which involves measuring the volume of gas evolved in the reaction of phenyldiazohydroxide with hydroquinone, was used more frequently.

SUMMARY

1. The kinetics for the decomposition of aliphatic aromatic triazenes in various media was studied.

2. The composition of the decomposition products of triazenes in water and water-hydrocarbon media was studied, and also in hydrocarbon media in the presence of organic acids.

3. The influence exerted by free radical acceptors on the composition of the decomposition products of triazenes was studied.

A mechanism for the process was discussed on the basis of experimental data.

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OXIDATION–REDUCTION SYSTEMS FOR THE INITIATION OF RADICAL PROCESSES

III. UTILIZATION OF THE REACTION FOR THE REDUCTION OF METAL OXIDE SALTS WITH HYDROCARBONS FOR INITIATION OF THE POLYMERIZATION PROCESS

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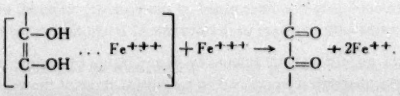
The significance of oxidation-reduction systems for the initiation of polymerization processes in aqueous emulsions is generally known. The oxidation-reduction systems for initiation of polymerization in a homogeneous (hydrocarbon) medium have been studied to a lesser degree.

The reaction between peroxides and the oxide salts of metals of variable valency can be used to induce polymerization in a homogeneous medium at a temperature of + 50°.

The more effective systems for the initiation of polymerization are created by the method of introducing reducing agents that are capable of converting the metal oxide salts into the protoxide salts at low temperatures.

Thus, Kern [1] was able to polymerize styrene at 40° by the use of a system composed of benzoyl peroxide, benzoin and ferric naphthenate. It was shown by Dolgoplosk, Tinyakova and others [2] that the system composed of isopropylbenzene hydroperoxide, diethyl dihydroxymaleate and ferric naphthenate is effective for the polymerization of styrene at 50°. A characteristic property of the reducing agents used in the indicated systems is their ability to form complexes with iron salts.

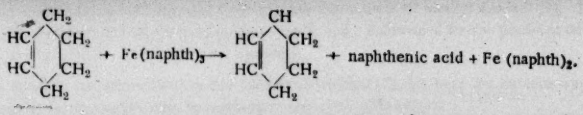
This circumstance, and also the impossibility of utilizing the reaction for the reduction of Fe^{+++} to Fe^{++} to initiate polymerization, indicate that the process apparently proceeds without the formation of free radicals, for example by the scheme:



Complexes of a similar type are excluded when hydrocarbons are used as the reducing agents. In this case it can be expected that the dehydrogenation of the hydrocarbon chain in the reduction of ferric iron to the ferrous state will be accompanied by the formation of free radicals, capable of initiating polymerization. The present investigation is devoted to a study of this problem.

EXPERIMENTAL AND DISCUSSION OF RESULTS

In connection with the desired reaction we selected the olefinic hydrocarbons as the reducing agents; for example, for cyclohexene:



We established that at 150° in the absence of oxygen the dimer of isoprene, 1,4-pentadiene, cyclohexene and normal amylene reduce ferric napthenate to ferrous naphthenate (Table 1).

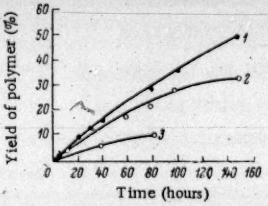


Fig. 1. Influence of the naphthenates of iron and chromium on the yield of polymer. 1) Fe^{+++} naphthenate (0.15 mole %), 2) Cr^{+++} naphthenate (0.15 mole %), 3) amount of Fe^{++} formed in % of the theoretical.

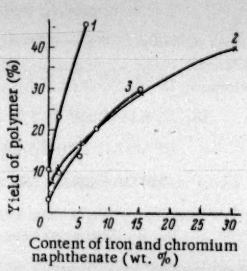


Fig. 2. Relationship between the yield of polymer and the amount of either iron or chromium naphthenate. Temperature 100°. 1) Fe^{+++} naphthenate (after 150 hours), 2) Fe^{+++} naphthenate (after 80 hours), 3) Cr^{+++} naphthenate (after 80 hours).

The formation of free radicals in the intermediate stages of the reaction was established on the basis of the polymerization effect.

We selected isoprene as the monomer, which in itself (or its dimeric forms) should possess the ability to behave as described above. It was established that at 100° ferric naphthenate initiates the homogeneous polymerization of isoprene. The polymerization process is accompanied by the transformation of the ferric naphthenate into ferrous naphthenate (Fig. 1). The rate of the polymerization process increases with increase in the ferric naphthenate concentration (Fig. 2).

For 8% naphthenate to monomer a 50% yield of polymer is obtained in 150 hours, in which connection the molecular weight of the obtained polymer, determined by the viscosity method, is 222,000. The molecular weight of the polymer increases with decrease in the amount of ferric naphthenate.

Under the polmerization conditions (100°) taken by us, any traces of oxygen, that might have remained in the system, should have been completely consumed in the initial stage of the process for the oxidation of the formed ferrous naphthenate. As had been shown [2], the oxidation of ferrous naphthenate by oxygen is practically instantaneous at room temperature.

In order to exclude the influence of possible traces of oxygen, which could have remained even after careful planning of the experiment, some experiments were performed in which additional ferrous naphthenate was added to the system.

As follows from the experimental data, the rate of the polymerization is determined only by the amount of ferric salts in the system.

The performed investigation permits making the conclusion that the process for the polymerization of isoprene under the influence of ferric naphthenate is conditioned by the formation of free radicals in the reaction

TABLE 1

Formation of Ferrous Naphthenate when Ferric Naphthenate Solutions are Heated. (Temperature 150°, duration 16 hours)

Reducing agent	Found Fe^{++} (%)
Cryoscopic benzene	2.8, 3.1
n-Amylene	6.5, 5.9
Isoamylene	7.8, 7.9
Cyclohexene	8.9, 9.2
1,4-Pentadiene	12.3, 12.5
Isoprene dimer	14.4, 12.8

TABLE 2

Influence of Ferrous Naphthenate on the Polymerization of Isoprene (Temperature 100°)

Time (hrs)	Amt. of naphthenate (wt.%) based on monomer		Yield of polymer (%)
	Fe^{+++}	Fe^{++}	
80	1.8	0.5	11.5
80	1.8	0	12
150	1.8	0.5	22.8
150	1.8	0	23

of ferric naphthenate with reducing agents, which in the given system can be the monomer, dimer or polymer of isoprene. A radical mechanism for the process is also supported by the structure of the obtained isoprene polymer. The amount of 1–2 and 3–4 links in the chain, found on the basis of the absorption spectra in the infrared region, is 5–6%, while the temperature at which the polymer forms a glass is 66.4°, which is in agreement with the results obtained in the polymerization of isoprene under the influence of free radicals.

The oxidation-reduction system containing trivalent chromium naphthenate gives a similar polymerization initiation effect. The yield of polymer, the same as in the case where ferric naphthenate is used, increases with increase in the chromium naphthenate concentration (Fig. 2).

The rate of the polymerization process in the presence of chromium naphthenate is somewhat slower than with ferric naphthenate (Fig. 1), which is in agreement with the oxidation-reduction potentials of these metals [3].

The isoprene dimer, cyclohexene, and other reducing agents shape the structure of the individual links of the various rubbers. In connection with this, it could be expected that reactions leading to the structural development of polymers, should take place when the rubbers are heated with ferric naphthenate in the absence of oxygen

$$-CH_2-C(CH_3)=CH-CH_2- + Fe(naphth)_3 \rightarrow$$
$$\rightarrow -CH-C(CH_3)=CH-CH_2- + Fe(naphth)_2 + \text{naphthenic acid.}$$

It is known that oxidation-reduction systems initiate not only polymerization processes, but also the processes for the construction (in the absence of oxygen) and destruction (in the presence of oxygen) of polymers [2]. These facts were also supported for the system studied by us.

An insoluble gel is formed when a 2% solution of polyisoprene in benzene is heated in the presence of ferric naphthenate for 16 hours at 150°. The construction process is accompanied by the transition of the ferric naphthenate into ferrous naphthenate. A solution of the polymer heated in the same manner in the absence of ferric naphthenate failed to suffer any noticeable changes. From this it follows that oxidation-reduction processes, leading to the construction of a polymer, and in the presence of oxygen to its destruction, can develop when rubbers are heated in the presence of hydrocarbon-soluble salts of metals with variable valence.

METHODS

a) The reaction of hydrocarbons with ferric napthenate was run in glass ampuls in the absence of oxygen.

The components of the system were introduced in measuring tubes, connected to the side openings of the ampuls. First the benzene solution of ferric naphthenate was introduced, the benzene was evaporated in vacuo, and then the hydrocarbon was introduced. The ampuls were sealed and placed in a thermostat, where they were heated for 16 hours at 150°.

After opening, 50% sulfuric acid was sucked into the ampuls, with previous evaporation in vacuo of unreacted hydrocarbons. After shaking with sulfuric acid, the ampul contents were poured into a separatory funnel in a nitrogen atmosphere. Then 10 ml of cryoscopic benzene was added. After short shaking the water layer was removed, diluted with water, and titrated with 0.1N potassium dichromate solution in the presence of diphenylamine. The sulfuric acid and benzene used in our work had been previously boiled and cooled in a stream of nitrogen.

b) The isoprene (fraction with b. p. 33.8–34°) used in the polymerization process had been previously treated with a saturated solution of potassium bisulfite, dried over calcium chloride and metallic sodium, and then distilled from metallic sodium. After purification, the isoprene was poured into vessel (A) (Fig. 3) in a countercurrent of nitrogen and then distilled into the graduate (B).

The benzene solution of ferric naphthenate was added to the ampul from tube (C), after which the benzene was evaporated in vacuo. Dosage of the isoprene was made through the tube attached to the neck of graduate (B). Then the ampul was sealed and placed in the thermostat at 100°.

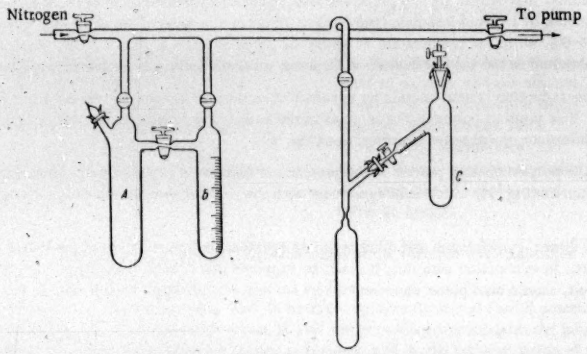


Fig. 3.

The yield of polymer was determined by precipitating it with methanol, washing the separated polymer, and drying it in vacuo at room temperature.

SUMMARY

1. It was established that olefinic hydrocarbons at 150°C reduce the hydrocarbon-soluble ferric salts to the ferrous salts.

2. It was shown that ferric and chromium naphthenates initiate the polymerization of isoprene in a homogeneous medium at 100°. During the polymerization process the ferric naphthenate is converted to ferrous naphthenate. The mechanism of this process is discussed.

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SYNTHESIS OF ETHYL ALCOHOL, CONTAINING THE HEAVY OXYGEN ISOTOPE

R. V. Kudryavtsev and D. N. Kursanov

Ethyl alcohol $C_2H_5O^{18}H$ is a key substance for obtaining a number of other organic compounds, containing the heavy oxygen isotope in a definite position in their molecule. Consequently, the synthesis of heavy-oxygen ethyl alcohol is of great interest, and the finding of a convenient method for the preparation of $C_2H_5O^{18}H$ would open up broader possibilities for the application of the heavy oxygen isotope to a study of the mechanisms of organic reactions.

Heavy-oxygen ethyl alcohol was first obtained by A. I. Brodsky in 1942 by the fractional distillation of ordinary alcohol through a multiplate column. However, this method can hardly be considered convenient, since it requires the presence of a special complicated apparatus and the large expenditure of time; in this connection the concentration of the heavy oxygen isotope in the obtained alcohol did not exceed 70–75 γ/cm^3.

In 1948, Lauder and Green [1] obtained small amounts of heavy-oxygen ethyl alcohol by the pressure hydrolysis of ethyl chloride with heavy-oxygen water.

At first we suggested obtaining heavy-oxygen ethyl alcohol by the oxidation of ethylmagnesium bromide. Model experiments (with ordinary oxygen) gave positive results; however, the yield of alcohol was very small. This caused us to seek other paths for the synthesis of ethyl alcohol containing the heavy oxygen isotope. It is known [2] that aldehydes enter into oxygen exchange reaction with water when brought in contact with it, even in the absence of catalysts and at room temperature:

$$R-C\begin{matrix}O^{16}\\H\end{matrix} + H_2O^{18} \rightleftarrows R-C\begin{matrix}O^{16}H\\|\\O^{18}H\\|\\H\end{matrix} \rightleftarrows R-C\begin{matrix}O^{18}\\H\end{matrix} + H_2O^{16}.$$

Acetaldehyde is miscible with water in all proportions. Oxygen exchange takes place when acetaldehyde is dissolved in heavy-oxygen water:

$$CH_3CHO^{16} + H_2O^{18} \rightleftarrows CH_3CHO^{18} + H_2O^{16}.$$

Exchange equilibrium is practically achieved in 24 hours. The expected concentration of the heavy oxygen isotope in the acetaldehyde after exchange can be calculated in advance by the use of the following formula:

$$\%\ O^{18}\ \text{in}\ CH_3CHO\ \begin{matrix}\text{after}\\\text{exchange}\end{matrix} = \frac{a \cdot N + b \cdot M}{a + b},$$

where a is the number of moles of CH_3CHO, b is the number of moles of H_2O^{18}, N = 0.204 is the concentration of O^{18} in the CH_3CHO (natural), and M is the concentration of O^{18} in the original water.

Pure dry acetaldehyde was mixed with the necessary amount of heavy-oxygen water and kept for a day. Then one drop of sulfuric acid was added and the acetaldehyde was distilled, after which it was hydrogenated in the gas phase [3] over skeletal nickel at 120–130°.

$$CH_3-C\begin{matrix}O^{18}\\H\end{matrix} \xrightarrow[Ni,\ 120-130^\circ]{H_2} C_2H_5O^{18}H.$$

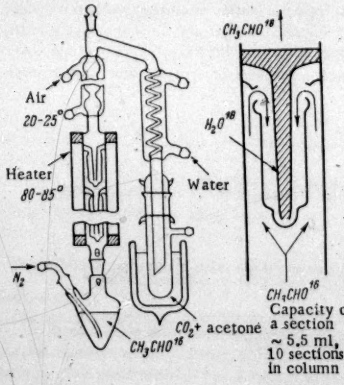
The catalyzate was again passed over the nickel under the same conditions. The yield of the alcohol was quantitative.

This method is apparently a general one for the preparation of various alcohols, enriched with the heavy oxygen isotope. However, its limitation is the impossibility of obtaining the aldehyde (and consequently, the alcohol) with the same O^{18} concentration as is present in the original water. To avoid this we constructed a special column, a schematic representation of which is shown in the Figure.

Heavy-oxygen water in the column is slightly acidified with sulfuric acid (1–2 drops for the whole column), which is simultaneously a catalyst for the oxygen exchange and a catalyst for the depolymerization of paraldehyde.

The acetaldehyde is passed through the column from the bottom to the top at 80–85°. Since the counterflow principle was partially realized in the column, then acetaldehyde with practically the same degree of heaviness as that possessed by the taken heavy-oxygen water was obtained when the passage rate of the acetaldehyde through the water was equal to 20–30 bubbles a minute. Evidently, this method of semicontinuous enrichment is suitable only for the aldehydes whose boiling points are considerably below the boiling point of water, for in the opposite case, the water will be carried out with the aldehyde, and the desired objective will not be achieved.

Butyl, amyl and other alcohols, containing O^{18}, can be obtained by the reduction of the corresponding aldehydes or ketones, enriched with the heavy oxygen isotope by a single exchange with H_2O^{18}.



Column for the preparation of labeled acetaldehyde.

EXPERIMENTAL

Into the column, shown in the Figure, was charged 62 ml of H_2O^{18} (O^{18} concentration in the water was 1.08%). Through this water at 80–85° acetaldehyde vapors were passed from the bottom to the top at a rate of 2–3 bubbles a second. After 16 hours 52 g of acetaldehyde, enriched with the heavy oxygen isotope, was obtained. Isotopic analysis of the acetaldehyde, made after 8 and 16 hours of operation, respectively, gave 1.06 and 1.10% O^{18}, which suggests practically complete "elution" of the O^{18} from the water by the acetaldehyde vapors.

The acetaldehyde prepared in this manner was passed in a hydrogen steam at 130° over skeletal nickel catalyst, prepared by the alkaline leaching of a 50% nickel-50% aluminum alloy. The catalyzate was again passed through the furnace under the same conditions. After being made absolute and distilling we obtained 47.4 g of $C_2H_5O^{18}H$.

B.p. 78-78.1° at 749 mm, $n_D^{19.5}$ 1.3620, d_4^{20} 0.7894, % O^{18} (in alcohol) 1.04%.

SUMMARY

Ethyl alcohol, containing the heavy oxygen isotope, was synthesized from acetaldehyde and heavy water.

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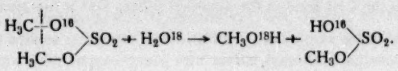
STUDY OF THE MECHANISM OF HYDROLYSIS BY MEANS OF THE HEAVY OXYGEN ISOTOPE

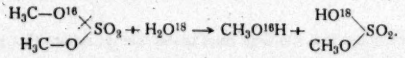
II. HYDROLYSIS OF DIMETHYL SULFATE IN ACID AND ALKALINE MEDIUM

D. N. Kursanov and R. V. Kudryavtsev

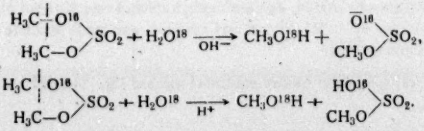
The purpose of the present investigation was to study the direction of bond rupture in the acid and alkaline hydrolysis of dimethyl sulfate. To hydrolyze the dimethyl sulfate we used water that had been enriched with the heavy oxygen isotope. If the C–O bond is ruptured in the hydrolysis of dimethyl sulfate, then the oxygen of the obtained methyl alcohol should be enriched with the heavy isotope:



If the S–O bond is ruptured in the hydrolysis, then the oxygen of the obtained methyl alcohol should show the normal (natural) isotopic ratio (0.2% O^{18}):



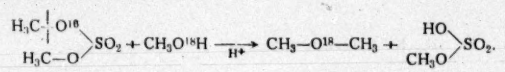
It was revealed that the hydrolysis of dimethyl sulfate in both alkaline and acid medium gave a methyl alcohol that showed a higher concentration of the heavy oxygen isotope. From this it follows that irrespective of whether dimethyl sulfate is hydrolyzed in alkaline or acid medium it is the C–O bond that is ruptured, and not the S–O bond:



However, it was also revealed that in both acid and alkaline medium, the concentration of the heavy oxygen isotope in the obtained methyl alcohol was less than in the water taken for the hydrolysis. This can be conditioned either by the fact that both the C–O and S–O bonds are simultaneously ruptured during hydrolysis, or by the fact that the hydrolysis is preceded by fairly rapid oxygen exchange between the water taken for hydrolysis and the oxygen in the sulfo group of dimethyl sulfate. The first explanation was adopted by Anbar, Dostrovsky, Samuel and Yoffe, who studied the mechanism of the alkaline hydrolysis of dimethyl sulfate [1]; however, the authors do not bring any data in support of this.

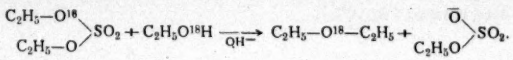
To elucidate this problem we ran the alkaline hydrolysis of dimethyl sulfate in a large excess of heavy-oxygen water and obtained a methyl alcohol with a considerably larger O^{18} content than in the first case. Taking into consideration the isotopic exchange of oxygen between the water and the ester, the O^{18} concentration in the methyl alcohol formed during hydrolysis agrees with the O^{18} concentration in the water taken for the hydrolysis. In addition, the O^{18} concentration in the unreacted water proves to be approximately equal to the O^{18} concentration in the obtained alcohol. From these data it follows that the second of the above-presented postulations is the correct one, which means that the hydrolysis of dimethyl sulfate is preceded by the isotopic exchange of the oxygen in the sulfo group.

In addition to the exchange reaction, a study of the mechanism for the hydrolysis of dimethyl sulfate in acid medium is complicated by the secondary reaction of alkylation of the formed methyl alcohol by the unreacted dimethyl sulfate:



It was revealed that both of the substances obtained in the acid hydrolysis of dimethyl sulfate, both the methyl alcohol and the dimethyl ether, show a substantial excess of the heavy oxygen isotope. In addition, it was revealed that the O^{18} concentration in the methyl alcohol, the dimethyl ether, and the unreacted water, coincide. This permits making two conclusions: first, that the acid hydrolysis of dimethyl sulfate proceeds with rupture of the C–O bond, and not of the S–O, and second, that in the acid alcoholysis of dimethyl sulfate by methyl alcohol it is again the C–O bond in the dimethyl sulfate that is ruptured, and not the S–O.

The mechanism of the alkaline alcoholysis of sulfuric acid esters was studied in 1948 by Lauder and Green [2], who showed that in the reaction of diethyl sulfate with heavy-oxygen ethyl alcohol the excess O^{18} migrates from the alcohol to the diethyl ether:



This means that in this case also it is the C–O bond in the diethyl sulfate that is ruptured, and not the S–O.

EXPERIMENTAL

1. Hydrolysis of Dimethyl Sulfate in Alkaline Medium.

In a 100-ml round-bottomed flask, fitted with a complete condensation head, thermometer, condenser and delivery tube, was placed 20 g of freshly distilled dimethyl sulfate (b. p. 100° at 42 mm), 9.36 ml of H_2O^{18} (containing 1.5% O^{18}) and 6.25 g of NaOH (c. p.). The O^{18} concentration in the mixture of water and sodium hydroxide was 1.2%. The mixture was heated, and the methyl alcohol was distilled off in measure with hydrolysis. The crude product was collected up to 75°, then it was distilled, and made absolute three times by distillation from small portions of calcium hydride.

The isotopic analysis was run by our earlier published method [3]. The O^{18} concentration in the obtained methyl alcohol was 0.82%.

2. Alkaline Hydrolysis of Dimethyl Sulfate With a Large Volume of Water

The experiment was run under the same conditions and in the same apparatus as the previous. Here we took 46.8 ml of H_2O^{18} (containing 1.5% O^{18}), 31.3 g of NaOH (c. p., 0.2% O^{18}) (as a result the O^{18} concentration in the mixture of H_2O^{18} and NaOH was 1.2%), and 23.0 g of dimethyl sulfate.

If two of the oxygen atoms in dimethyl sulfate exchange with the oxygen in the water and NaOH the O^{18} content in each substance will be 1.09%.

The mixture was heated on the water bath with stirring. Then the methyl alcohol and part of the water was vacuum-distilled (the receiver was cooled in liquid nitrogen). The methyl alcohol was distilled from the

water at atmospheric pressure (to 80°), and then made absolute by a 3-fold distillation from calcium hydride. The obtained alcohol had m. p. 63.5–64°. The O^{18} concentration in the obtained methyl alcohol was 1.16%.

3. Hydrolysis of Dimethyl Sulfate in Acid Medium.

We took 20.0 g of dimethyl sulfate and 7.0 ml of H_2O^{18} for the hydrolysis. The mixture was acidified with a small amount (~0.01 g) of sulfuric acid and warmed slightly on the air bath. The dimethyl ether passed through the water-cooled condenser, and condensed in the trap cooled with the liquid nitrogen. The O^{18} concentration in the dimethyl ether was 1.08%. In addition to the dimethyl ether, we were able to isolate a small amount of methyl alcohol. The O^{18} content in the alcohol was 1.01%.

SUMMARY

1. The mechanism of the acid and alkaline hydrolysis of dimethyl sulfate was studied. It was shown that the hydrolysis of dimethyl sulfate proceeds with rupture of the C–O bond. The S–O bond remains untouched.

2. The mechanism for the alkylation of methyl alcohol by methyl sulfate in acid medium was studied. It was shown that here it is the C–O bond in dimethyl sulfate that suffers rupture.

3. It was revealed that oxygen in the sulfo group of dimethyl sulfate is capable of exchange.

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LOW TEMPERATURE OXIDATION OF METHANE HYDROCARBONS

B. G. Gavrilov and G. V. Zinovyeva

The most probable final reason for the detonation of hydrocarbon motor fuels in internal combustion engines with spark ignition is the peroxides that arise in the period preceding the bulk burning of the fuel.

A study of the quantitative characterization of oxidizability in general and of the formation of peroxides, in particular, by the hydrocarbons of benzine distillates, under similar conditions, brings us closer to an understanding of the reasons for detonation.

The majority of the studies on the oxidation of hydrocarbons, run under various conditions, have as their goal a careful characterization of the obtained oxidation products. The classic studies in this field are those of K. I. Ivanov [1] and co-workers, who studied the structure and chemical properties of the formed organic peroxides. At the same time they demonstrated the most vulnerable spots in the hydrocarbon molecules for the attacking oxygen. S. E. Krein [2] studied the oxidation of various classes of hydrocarbons. The degree of oxidation was determined by the amount of absorbed oxygen, and also by the magnitude of the acid number and the saponfication number. It was shown by Krein that the degree of branching possessed by aliphatic hydrocarbons exerts a beneficial effect on their oxidizability. Other authors [3, 4] studied the oxidation of methane hydrocarbons ranging from C_3 to C_8 at relatively high temperatures of the order of 300–600°.

EXPERIMENTAL

The method selected by us pursued the goal of retaining the structures of the taken hydrocarbons and initially formed oxygen compounds, avoiding the formation of gaseous oxidation products, and retaining a uniformity of the experimental conditions.

The oxidation was run at 50° in a quartz test tube with ultraviolet illumination from a PRK-2 lamp. The amount of O was carefully measured with a rheometer and was 10 ml/min. The duration of oxidation was 100 hours. The amount of hydrocarbons in each experiment was 35 ml. The quartz test tube was placed 20 cm away from the lamp. Above the test tube in the thermostat, was placed an efficient reflux coil condenser, 1 meter in length. In all of the experiments, the unbound oxygen was checked for its content of carbon-containing gases, the presence of which was not revealed.

The percent content of hydroperoxides, acids, carbonyl compounds and active hydrogen was determined in the oxidized hydrocarbons. The quantitative content of peroxide oxygen was determined by the method of T. Kasterina and M. Itkina [5]. The acids were determined by the titration of a hydrocarbon sample with 0.1N sodium hydroxide solution in the presence of phenolphthalein. Determination of carbonyl-containing compounds via the oximes gave no positive results; consequently, we had to resort to the spectrophotometric method, which proved suitable for our conditions [6]. Active hydrogen was determined by the Chugaev-Tserevitinov method.

The general results of the study are summarized in the Table.

Hydrocarbon	Boiling point	d_4^{20}	n_D^{20}	Hydroperoxide O (%)	Carboxyl O (%)	Alc. & water O (%)	Active (total) H (%)	Carbonyl O (%)	Total combined O (%)	Total O (% on 1 mole)
n-Hexane	68.5°	0.6609	1.3750	0.03	0.07	1.85	1.12	1.83	3.77	3.24
2,3-Dimethylbutane	58.2	0.6622	1.3748	0.21	0.49	2.00	0.157	2.06	4.77	4.10
n-Heptane	98.0	0.6830	1.3874	0.04	0.11	3.97	0.25	0.95	4.98	4.98
2-Methylhexane	89.5	0.6890	1.3854	0.09	0.27	4.61	0.30	1.31	6.28	6.29
n-Octane	124.5	0.7022	1.3970	0.02	0.05	2.87	0.18	0.96	3.91	4.45
2,5-Dimethylhexane	109.8	0.6952	1.3930	3.04	0.32	2.97	0.29	0.40	6.73	7.67
2,2,4-Trimethylpentane	99.8	0.6923	1.3912	0.02	0.04	1.37	0.09	0.14	1.58	1.80
n-Nonane	149.5	0.7166	1.4050	0.02	0.07	1.2	0.07	0.40	1.70	2.17

SUMMARY

1. A quantitative study was made of the oxidation capacity shown by the benzine fraction hydrocarbons: n-hexane, 2,3-dimethylbutane, n-heptane, 2-methylhexane, n-octane, 2,5-dimethylhexane, 2,2,4-trimethylpentane and n-nonane in the liquid phase under the influence of oxygen and with photochemical forcing by ultraviolet light.

2. It was shown that all of the hydrocarbons of iso structure, with the exception of 2,2,4-trimethylpentane, have a greater oxidation capacity than the corresponding normal analogs.

3. As a rule, in the homologous series of normal hydrocarbons ranging from hexane to nonane the capacity shown by the hydrocarbons for oxidation decreases with increase in the molecular weight.

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CONJUGATED SYSTEMS

LXIX. DIENE SYNTHESES WITH FLUOROPRENE. II. CONDENSATION OF FLUOROPRENE WITH DERIVATIVES OF α,β-UNSATURATED MONOBASIC ACIDS

A. A. Petrov and A. V. Tumanova

In the previous paper we communicated on the condensation of fluoroprene with α,β-unsaturated aldehydes and ketones [1]. Continuing our studies in this direction, we studied the condensation of fluoroprene with the derivatives of some α,β-unsaturated monobasic acids – with the esters of acrylic and methacrylic acids and with acrylonitrile.

Corresponding syntheses with the participation of chloroprene have been described in the literature, in which connection it was shown that the condensation products (when derivatives of acrylic acid were involved) have a structure corresponding to the general formula A, where X = COOH, COOR or CN [2–4].

A

On this basis we assigned to the products obtained in the condensation of fluoroprene with the derivatives of unsaturated acids the same general formula of para-substituted cyclohexene derivatives.

The condensation of fluoroprene with methyl acrylate gave us the methyl ester of 4-fluorocyclohexene-3-carboxylic acid (I). Saponification of (I) gave the crystalline acid (II). Acid (II) was converted to the chloride (III) by treatment with thionyl chloride. Treatment of chloride (III) with ammonia gave the crystalline amide (IV), while treatment of (III) with methyl alcohol gave the starting methyl ester (I).

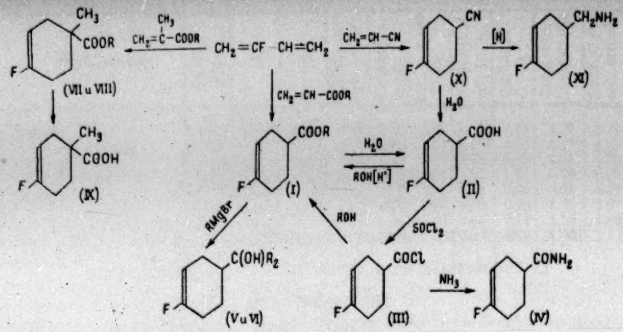
In addition, the reaction of ester (I) with methylmagnesium iodide gave the tertiary alcohol (V), described by us earlier, while its reaction with ethylmagnesium iodide gave the tertiary alcohol (VI). Dehydration of (V) gave the fluorohydrocarbon, boiling in quite a wide temperature range. The dehydrogenation of the latter on platinum gzve a mixture of cumene and fluorocumene, the oxidation of which gave a mixture of benzoic and fluorobenzoic acids.

The condensation of fluoroprene with methyl and butyl methacrylates gave the corresponding esters of 4-fluoro-1-methylcyclohexene-3-carboxylic acid (VII and VIII). Saponification of methyl ester (VII) gave the crystalline acid (IX).

Further from fluoroprene and acrylonitrile we obtained the nitrile (X) of acid (II). Saponification of nitrile (X) led to acid (II) with the same constants as the acid obtained from the methyl ester (I). The reduction of (X) with metallic sodium in alcohol gave 4-fluoro-Δ^3-tetrahydrobenzylamine (XI). Under the same conditions the similarly constructed nitrile, obtained from chloroprene, is reduced with the loss of the chlorine atom. The dehydrogenation of (X) with bromine and alkali gave a mixture of benzoic and fluorobenzoic acids.

The transformations of fluoroprene described in this paper are schematically depicted below.

A comparison of the experimental results obtained on the condensation of fluoroprene and chloroprene with the derivatives of α,β-unsaturated monobasic acids reveals that the formation of polymeric and secondary products is usually observed to a less degree for the fluoroprene.



(V) + (VII) R = CH_3; (VI) R = C_2H_5; (VIII) R = C_4H_9

EXPERIMENTAL

1. Condensation of Fluoroprene With Methyl Acrylate

A solution of 36 g (0.5 mole) of fluoroprene, stabilized with p-tert-butylpyrocatechol, and 43 g (0.5 mole) of freshly distilled methyl acrylate in 20 ml of toluene was heated at 140° for 10 hours. The toluene and unreacted starting substances were then distilled off, and the reaction product was vacuum-distilled. We obtained 46.3 g (59%) of methyl 4-fluorocyclohexene-3-carboxylate (I) as a pleasant smelling liquid.

B.p. 109–110° (50 mm), d_4^{20} 1.1239, n_D^{20} 1.4460, MR_D 37.52; calc. 38.03.
Found %: F 11.63; OCH_3 19.66. $C_8H_{11}O_2F$. Calculated %: F 12.01; OCH_3 19.60.

A solution of 24 g of KOH in 100 ml of water was used to saponify 32 g of (I). The obtained solution of salts was evaporated on the water bath and acidified with 50% sulfuric acid. The oil was separated, and the water solution was extracted with ether. The oil and ether extracts were combined and dried over Na_2SO_4. The ether was distilled off and the 4-fluorocyclohexene-3-carboxylic acid (II) was vacuum-distilled. Yield 26.6 g (92%).

B.p. 140–141° (20 mm). After distillation the acid crystallized. M.p. 39–40°.
Found %: F 13.09. Equiv. 143.7. $C_7H_9O_2F$. Calculated %: F 13.10. Equiv. 144.1.

To 22 g of acid (II) was added in small portions 23 g of thionyl chloride and then the mixture was heated on the water bath until SO_2 and HCl ceased to evolve. We obtained 19.4 g (78%) of the chloride of 4-fluorocyclohexene-3-carboxylic acid (III).

B.p. 87.5–88.5° (20 mm), d_4^{20} 1.2403, n_D^{20} 1.4716, MR_D 36.53; calc. 36.63.
Found %: Cl 21.70. C_7H_8OFCl. Calculated %: Cl 21.84.

Fifteen grams of chloride (III) was added (in drops) to 100 ml of a well-stirred 25% ammonia solution, cooled in a cooling mixture of ice and salt. The obtained crystals of 4-fluorocyclohexene-3-carboxamide (IV) were suction-filtered, washed with water, and dried in a desiccator over P_2O_5. Yield 6.8 g (52%). After recrystallization from water the amide (IV) melted at 149°.

Found %: N 9.73. $C_8H_{10}ONF$. Calculated %: N 9.87.

Two grams of chloride (III) was heated for 20 minutes with 1.5 ml of methyl alcohol under reflux. The mixture was diluted with water, the oily layer separated, and then washed with saturated $CaCl_2$ solution. Methyl 4-fluorocyclohexene-3-carboxylate (I) was obtained.

B.p. 109–110° (20 mm), n_D^{20} 1.4470.
Found %: OCH_3 19.50. $C_8H_{11}O_2F$. Calculated %: OCH_3 19.61.

To the Grignard reagent from 21.1 g of magnesium and 124 g of methyl iodide was added an ether solution of 46 g of methyl ester (I). After the mixture was heated on the water bath for 1 hour the complex was decomposed with a mixture of ice and saturated NH_4Cl solution. The ether layer and the ether extracts of the water layer were worked up in the usual manner. The yield of dimethyl-(4-fluoro-3-cyclohexenyl)-carbinol (V) was 30.3 g (66%).

B.p. 92–93.5° (10 mm), d_4^{20} 1.0492, n_D^{20} 1.4680, MR_D 41.86; Calc. 41.62.

Found %: F 12.28; OH 10.73, 10.30. $C_9H_{15}OF$. Calculated %: F 12.02; OH 10.74.
The constants given earlier for alcohol (V) were [1]: B.p. 108–109° (20 mm), d_4^{20} 1.0478, n_D^{20} 1.4680.

The heating of 34.4 g of alcohol (V) with 50 ml of acetic anhydride at 220° for 2 hours gave, after the usual treatment of the mixture, about 24 g of oil, the distillation of which gave 14.8 g (49%) of fluorohydrocarbon (presumably 2-fluoroisopropenyl-3-cyclohexene).

B.p. 64–66° (20 mm), d_4^{20} 0.9607, n_D^{20} 1.4640, MR_D 40.26; calc. 40.53.
Found %: F 13.45. $C_9H_{13}F$. Calculated %: F 13.50.

The dehydrogenation of the substance on platinized charcoal at 300° gave about 12 g of a mixture of cumene and fluorocumene.

B.p. 150–154°, d_4^{20} 0.8885, n_D^{20} 1.4848.

The substance contained about 3% fluorine, instead of the 13.7% calculated for fluorocumene, and when oxidized with dilute nitric acid it gave a mixture of benzoic and fluorobenzoic acids with a melting range of 122–150°. After three recrystallizations this mixture gave the following fractions: 1st. 122–135°, 2nd. 141–149°. 3rd. 164–173°. When potassium permanganate was used to oxidize the starting mixture we were able to obtain a purer benzoic acid with m.p. 120–122°.

The reaction of 20 g of ester (I) with an ether solution of ethylmagnesium bromide (from 9.1 g of magnesium and 42 g of ethyl bromide) gave 16 g (68%) of diethyl-4-fluoro-3-cyclohexenyl)-carbinol (VI).

B.p. 117–118° (10 mm), 131–132° (20 mm), d_4^{20} 1.0364, n_D^{20} 1.4750, MR_D 50.60; Calc. 50.53.
Found %: F 10.00; OH 8.85, 9.06. $C_{11}H_{19}OF$. Calculated %: F 10.20; OH 9.13.

The dehydration of the alcohol with acetic anhydride under the earlier described conditions gave a mixture of fluorohydrocarbons with b.p. 90–100° (20 mm). For the main fraction we obtained:

B.p. 96–97° (20 mm), d_4^{20} 0.9458, n_D^{20} 1.4687, MR_D 50.10. $C_{11}H_{17}F$. Calc. 49.76.

2. Condensation of Fluoroprene With Methyl Methacrylate

A solution of 14.5 g (0.2 mole) of fluoroprene, 20 g (0.2 mole) of freshly distilled methyl methacrylate and 0.25 g of hydroquinone in 20 ml of toluene was heated at 150° for 14 hours. We obtained 12.7 g (39%) of methyl 4-fluoro-1-methylcyclohexene-3-carboxylate (VII) with b.p. 85–89° (20 mm) and 22 g of polymers. After redistillation the ester (VII) had the constants:

B.p. 88.5–89° (20 mm), d_4^{20} 1.0880, n_D^{20} 1.4468, MR_D 42.26; Calc. 42.65.
Found %: F 11.34; OCH_3 17.73. $C_9H_{13}O_2F$. Calculated %: F 11.03; OCH_3 18.02.

The saponification of ester (VII) (boiling with aqueous KOH solution and subsequent acidification with H_2SO_4) gave 4-fluoro-1-methylcyclohexene-3-carboxylic acid (IX). Long needles. Readily soluble in the ordinary organic solvents.

B.p. 141–142° (20 mm), M.p. 41–42°.
Found Equiv. 157. $C_8H_{11}O_2F$. Calculated Equiv. 158.

3. Condensation of Fluoroprene With Butyl Methacrylate

A solution of 14.5 g (0.2 mole) of fluoroprene, 28.5 g (0.2 mole) of freshly distilled butyl methacrylate and 0.5 g of hydroquinone in 30 ml of toluene was heated at 150° for 14 hours. We obtained 7.9 g of butyl 4-fluoro-1-methylcyclohexene-3-carboxylate (VIII).

B.p. 123–124° (20 mm), d_4^{20} 1.0163, n_D^{20} 1.4451, MR_D 56.12; Calc. 56.50.
Found %: F 8.48. $C_{12}H_{19}O_2F$. Calculated %: F 8.83.

4. Condensation of Fluoroprene With Acrylonitrile

A solution of 14.5 g (0.2 mole) of fluoroprene, 10.6 g (0.2 mole) of acrylonitrile and 0.2 g of hydroquinone in 40 ml of toluene was heated at 140° for 10 hours. We obtained 14.4 g (58%) of the nitrile of 4-fluorocyclohexene-3-carboxylic acid (X).

B.p. 100.5° (20 mm), d_4^{20} 1.0875, n_D^{20} 1.4570, MR_D 31.34; Calc. 31.57.
Found %: F 15.61; N 11.38. C_7H_8NF. Calculated %: F 15.18; N 11.20.

The nitrile (X) (7.5 g) was heated with a solution of 10.7 g of NaOH in 11 ml of water and 33 ml of ethyl alcohol. When ammonia ceased to evolve, the alcohol was evaporated in vacuo and the residue was acidified with excess 50% sulfuric acid. The 4-fluorocyclohexene-3-carboxylic acid (II) was extracted with ether. Yield 8.4 g (97%).

B.p. 140.5–141° (20 mm), M.p. 39–40°.
Found %: F 12.80. Equiv. 142.7, 145.5. $C_7H_9O_2F$. Calculated %: F 13.10. Equiv. 144.1.

To a boiling solution of 5 g of nitrile (X) in 50 ml of ethyl alcohol was added through the reflux condenser in small pieces 9 g of metallic sodium. When the sodium had dissolved the flask was cooled and its contents diluted with water. The alcohol was distilled through a column. The 1'-amino-1-methyl-4-fluoro-3-cyclohexene (4-fluoro-Δ^3-tetrahydrobenzylamine) (XI) was extracted with ether. Yield 3.5 g (69%).

B.p. 98° (20 mm), 174–175° (760 mm), d_4^{20} 1.0235, n_D^{20} 1.4633, MR_D 35.10; Calc. 35.18.
Found %: N 10.57. $C_7H_{12}NF$. Calculated %: N 10.84.

SUMMARY

1. The reactions of fluoroprene with methyl acrylate, methyl methacrylate, butyl methacrylate and acrylonitrile were studied.

2. The 4-fluoro- and 4-fluoro-1-methylcyclohexene-3-carboxylic acids were described, as were also the methyl ester, chloride, amide and nitrile of the first acid and the methyl and butyl esters of the second acid.

3. The reduction of the nitrile of 4-fluorocyclohexene-3-carboxylic acid gave 4-fluoro-Δ^3-tetrahydrobenzylamine.

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CONJUGATED SYSTEMS

LXX. DIENE SYNTHESES WITH FLUOROPRENE. III. CONDENSATION OF FLUOROPRENE WITH THE ESTERS OF α,β-UNSATURATED DIBASIC ACIDS

A. A. Petrov and A. V. Tumanova

In the two preceding papers we had shown that fluoroprene easily enters into various condensation reactions with α,β-unsaturated aldehydes, ketones and the derivatives of monobasic acids – the esters and nitriles [1, 2]. The present communication is devoted to a study of the condensation of fluoroprene with the esters of the α,-β-unsaturated dibasic acids.

We investigated the reactions of fluoroprene with the methyl and ethyl esters of maleic, fumaric and acetylenedicarboxylic acids. In all cases the formation of the desired condensation products was observed – the esters of the corresponding fluorocyclohexene- and fluorocyclohexadienedicarboxylic acids. Saponification of these esters gave the corresponding acids. 4-Fluorocyclohexene-4-dicarboxylic acid is described in the literature. It was obtained by the hydrolysis of the condensation product of fluoroprene with maleic anhydride [3].

The constants of the obtained substances are compared in the Table, from which it can be seen that the esters of fluorodihydrophthalic acid boil above the esters of fluorotetrahydrophthalic acid and also show a higher specific gravity and index of refraction.

EXPERIMENTAL

Condensation of Fluoroprene With Maleic Acid Esters.

a) A solution of 7.2 g (0.1 mole) of fluoroprene and 14.4 g (0.1 mole) of dimethyl maleate in 30 ml of toluene (+hydroquinone) was heated at 150° for 13 hours.

Vacuum-distillation of the mixture gave 10.5 g (49%) of the dimethyl ester of 4-fluorocyclohexene-4-dicarboxylic acid. Colorless oily liquid with a pleasant odor. The constants of this and the later described esters are given in the Table.

Found %: F 8.72; OCH_3 28.50. $C_{10}H_{13}O_4F$. Calculated %: F 8.79; OCH_3 28.71.

The ester (2.6 g) was heated with a solution of 3.5 g of KOH in 50 ml of water under reflux for 2 hours. The reaction mixture after cooling was acidified with 25% sulfuric acid and the organic acid was extracted with ether. A crystalline mass remained when the ether was distilled off. The substance was recrystallized from a mixture of ethyl acetate and petroleum ether. M. p. 158–159°. Literature [3]: m. p. 163°.

b) From 7.2 g of fluoroprene and 17.2 g of diethyl maleate under the same conditions we obtained 12.2 g of the diethyl ester of 4-fluorocyclohexene-4-dicarboxylic acid.

Found %: F 8.04; OC_2H_5 36.48. $C_{10}H_{17}O_4F$. Calculated %: F 7.78; OC_2H_5 36.89.

Substance		Boiling point at pressure (in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
	Cis	130—131° (10) 145—147 (20)	1.2184	1.4590	48.00	48.92
	Trans	129—130 (10) 144—145 (20)	1.2086	1.4572	48.74	48.92
	Cis	144—145 (10) 158—159 (20)	1.1386	1.4552	58.22	58.15
	Trans	140 (10) 155 (20)	1.1308	1.4530	58.05	58.15
		138.5—139 (10)	1.2524	1.4805	48.58	48.48
		150—150.5 (10)	1.1735	1.4712	57.66	57.69

Condensation of Fluoroprene With Fumaric Acid Esters.

a) From 7.2 g of fluoroprene and 14.4 g of crystalline dimethyl fumarate in 30 ml of toluene was obtained 10.0 g of the dimethyl ester of trans-4-fluorocyclohexene-4-dicarboxylic acid.

Found %: F 8.76, 9.13; OCH_3 28.47. $C_{10}H_{13}O_4F$. Calculated %: F 8.79; OCH_3 28.71.

b) From 7.2 g of fluoroprene and 17.2 g of diethyl fumarate was obtained 11.4 g of the diethyl ester of trans-4-fluoro-cyclohexene-4-dicarboxylic acid.

Found %: F 8.03, 8.06; OC_2H_5 36.57. $C_{12}H_{17}O_4F$. Calculated %: F 7.78; OC_2H_5 36.89.

Condensation of Fluoroprene With Acetylenedicarboxylic Acid Esters.

Acetylenedicarboxylic acid was prepared from fumaric acid through dibromosuccinic acid.

a) A mixture of 20 g of acetylenedicarboxylic acid, 75 ml of anhydrous methanol and 3 g of concentrated sulfuric acid was heated under reflux on the water bath for 3 hours. Then half of the alcohol was distilled off, the residue was diluted with water, the ester layer separated, and the water layer extracted with ether. The oil and ether extracts were combined, washed with $CaCl_2$ solution, and dried over Na_2SO_4. We obtained about 9 g of the dimethyl acetylenedicarboxylate.

B.p. 97—98° (20 mm), n_D^{20} 1.4478.
Literature [4]: B.p. 102—103.3° (20 mm).

The heating of 3.6 g (0.05 mole) of fluoroprene with 7.1 g (0.05 mole) of dimethyl acetylenedicarboxylate in 10 ml of toluene in sealed tubes at 120—125° for 7 hours gave 8.7 g (81%) of the dimethyl ester of 4-fluoro-cyclohexadiene-1,4-dicarboxylic acid. A colorless liquid with very little odor.

Found %: OCH_3 28.92. $C_{10}H_{11}O_4F$. Calculated %: OCH_3 29.06.

The obtained ester (1 g) was saponified with KOH solution (1.5 g of KOH in 15 ml of water), the solution was acidified with sulfuric acid, and the organic acid was extracted with ether. Removal of the ether by distillation gave a crystalline residue. The 4-fluorocyclohexadiene-1,4-dicarboxylic acid was purified by its precipitation from ethyl acetate solution with petroleum ether. M. p. 170°.

Found Equiv. 187.2. $C_8H_7O_4F$. Calculated Equiv. 186.1.

b) The diethyl ester of acetylenedicarboxylic acid was prepared in the same manner as the dimethyl ester.

B.p. 118–120° (20 mm), d_4^{20} 1.0735, n_D^{20} 1.4428.
Literature [4]: B.p. 120–122° (27 mm), d_4^{20} 1.0653, n_D^{20} 1.4405.

From 2.2 g (0.03 mole) of fluoroprene and 3.4 g (0.02 mole) of diethyl acetylenedicarboxylate under the above described conditions we obtained 3.5 g (82%) of the diethyl ester of 4-fluorocyclohexadiene-1,4-dicarboxylic acid.

Found %: F 7.51. $C_{12}H_{15}O_4F$. Calculated %: F 7.80.

SUMMARY

1. The condensation of fluoroprene with the dimethyl and diethyl esters of maleic, fumaric and acetylenedicarboxylic acids was studied.

2. The methyl and ethyl esters of cis- and trans-4-fluorocyclohexene-4-dicarboxylic acid and 4-fluorocyclohexadiene-1,4-dicarboxylic acid were described.

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REACTION OF CYCLOPROPANE HYDROCARBONS WITH MERCURIC SALTS

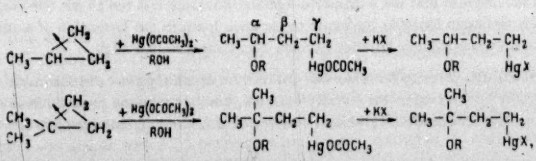
V. ACTION OF MERCURIC ACETATE ON METHYLCYCLOPROPANE AND 1,1-DIMETHYLCYCLOPROPANE

R. Ya. Levina, V. N. Kostin and V. A. Tartakovsky

In our previous studies we described a new reaction – the opening of the three-membered ring in alkylcyclopropanes (1,1,2,2-tetramethylcyclopropane [1, 2], 1,1,2-trimethylcyclopropane [3] and 1,1,2-trimethyl-2-ethylcyclopropane [4]) under the influence of mercuric acetate. The reaction was run in water, methanol and ethanol solutions, with cooling (from 0 to -5°) and periodic shaking.

In the present investigation we studied the influence of mercuric acetate in water and methanol solutions on the simplest alkylcyclopropanes – 1,1-dimethylcyclopropane and methylcyclopropane, for which a relatively stable ring is characteristic.

It was found that for successful reaction here somewhat more drastic conditions were required – room temperature (18–20°) and constant shaking of the reaction mixture on a mechanical shaker for 10–12 hours in the case of the 1,1-dimethylcyclopropane, and for 20 hours in the case of the methylcyclopropane. The 3-hydroxy and 3-methoxyalkylmercury acetates formed under these conditions are viscous oils; when subsequently treated with various potassium salts they gave a series of crystalline organomercury compounds, which can be utilized for the identification of methylcyclopropane and 1,1-dimethylcyclopropane:



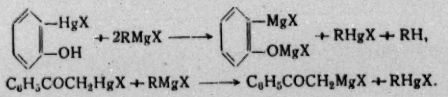
where OR = OH и OCH_3; X = Cl, Br, I, CN or CNS.

The structure of the γ-mercurated alcohols, obtained from the two hydrocarbons (and consequently the point of cleavage of the three-membered ring), was established by reduction – replacement of the HgX group (X = Cl) by hydrogen.

In an attempt to find a more convenient method for the reduction of 3-hydroxyalkylmercury salts than the earlier used treatment with sodium amalgam in water [1–4], we investigated their reaction with ethylmagnesium bromide.

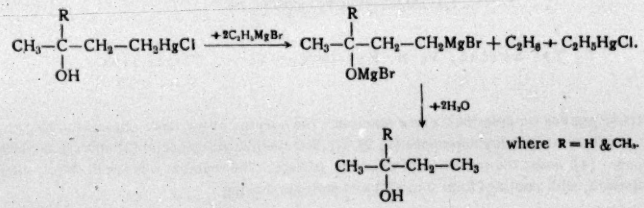
In 1941, A. N. Nesmeyanov and K. A. Pecherskaya established that the halomercury group, found in the α-position to the carbonyl group or in the ortho-postion to the phenol hydroxyl, is replaced by the magnesial

radical of the Grignard reagent. For example, mercurated phenol and mercurated acetophenone behave in this manner [5, 6]:



$$C_6H_5COCH_2HgX + RMgX \longrightarrow C_6H_5COCH_2MgX + RHgX.$$

It was revealed that the γ-mercurated alcohols, obtained from methyl- and 1,1-dimethylcyclopropane, are also capable of this exchange reaction; when decomposed with water the formed organomagnesium compounds were converted into the respective alcohols, namely sec-butyl and tert-amyl alcohols; in both cases ethylmercury chloride was isolated from the reaction mixture:•



where R = H & CH_3.

The obtained alcohols were identified as the crystalline 3,5-dinitrobenzoates; the mixed melting points of the latter with the 3,5-dinitrobenzoates from authentic sec-butyl and tert-amyl alcohols were not depressed.

The formation of sec-butyl and tert-amyl alcohols as the solitary reduction products of γ-mercurated alcohols showed that the opening of the three-membered ring in methylcyclopropane and 1,1-dimethylcyclopropane occurs at the most highly polarized bond, between the alkylated and nonalkylated carbon atoms of the ring.

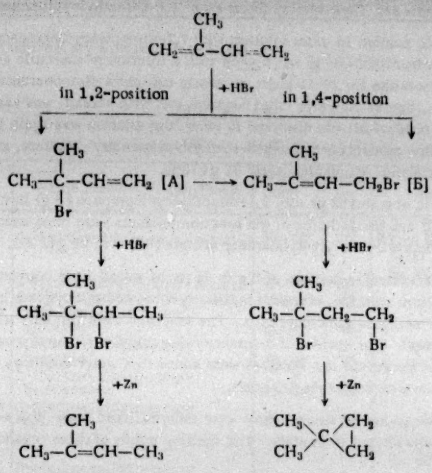
1,1-Dimethylcyclopropane was synthesized by the method that one of us had developed earlier [7], i. e., by the exhaustive hydrobromination of isoprene and subsequent treatment of resulting 1,3-dibromide with zinc dust; the method was modified in that the exhaustive hydrobromination was run in not one stage, but in two. The addition of the first hydrogen bromide molecule to isoprene leads to the formation of a mixture of the two unsaturated monobromides – the tertiary bromide (A) and the primary bromide (B).

Of these two bromides, the primary bromide was suitable for obtaining the 1,3-dibromide, later being converted to the cyclopropane hydrocarbon; the tertiary bromide, adding hydrogen bromide in accord with the Markovnikov rule, forms the 1,2-dibromide, which is converted into the ethylene hydrocarbon when treated with zinc dust.

To isolate the primary monobromide (B) in a pure state, the obtained mixture of monobromides was vacuum-distilled; here the tertiary bromide was isomerized to the primary bromide [8], which was later reacted with a second molecule of hydrogen bromide.

Judging from the Raman spectrum, the 1,1-dimethylcyclopropane obtained in this manner, after distillation through a column, failed to contain any unsaturated hydrocarbons as impurities.

•The 3-hydroxyalkylmercury chlorides, obtained from 1,1,2-trimethylcyclopropane and 1,1,2,2-tetramethylcyclopropane, react with ethylmagnesium bromide in a similar manner.



EXPERIMENTAL

1,1-Dimethylcyclopropane. Hydrogen bromide was added to 150 g of isoprene (under cooling with ice and salt) until the weight increase was 180 g; each hydrobromination experiment was run with 20 g of isoprene. The obtained mixture of monobromides was let stand for a day at room temperature, and then was distilled twice at 70 mm; the fraction with b. p. 60–65° was collected; yield 270 g (82%).

Literature data [8] for the primary hydrobromide of isoprene (1-bromo-3-methyl-2-butene): b. p. 50–60° (65 mm).

The second hydrogen bromide molecule was added under the same conditions. The obtained 1,3-dibromo-3-methylbutane was dried over calcium chloride and vacuum-distilled; yield 365 g (88%).

B.p. 70° (10 mm), n_D^{20} 1.5062. Literature [9]: B.p. 80–82° (23 mm).

To 450 g of zinc dust in 1 liter of 75% ethyl alcohol with heating on the water bath (70–80°) and vigorous stirring was added in drops an alcohol solution (1:1) of 365 g of 1,3-dibromo-3-methylbutane. In measure with adding the dibromide the formed dimethylcyclopropane was distilled from the reaction mixture, and passing through a reflux condenser and coil, cooled with ice and salt, was collected in the receiver. The addition of the dibromide to the zinc dust was regulated by the distillation rate of the hydrocarbon. The obtained 1,1-dimethylcyclopropane was shaken with a 1% permanganate solution, cooled to 0°, and then was distilled twice from sodium (through a column). Yield 75 g (68%).

B.p. 20–21° (748 mm) n_D^{20} 1.3658, d_4^{20} 0.6671. Literature [10]: B.p. 19.8° (740 mm), n_D^{20} 1.3656, $d_4^{14.4}$ 0.6681.

Methylcyclopropane. The synthesis of methylcyclopropane by the treatment of 1,3-dibromobutane (200 g) with zinc dust (240 g) was run by the method described above (the formed gaseous methylcyclopropane was passed through 1% permanganate solution; the coil and receiver were cooled with dry ice); yield 44.6 g (85%).

Literature [11]: B.p. 4–5°.

A study of the Raman spectra• revealed that the obtained cyclopropane hydrocarbons fail to contain ethylene hydrocarbons as impurities.

•We wish to thank E. G. Treshcheva and P. A. Akishin for running the optical studies.

1. γ-Mercurated Alcohols and Their Methyl Esters From 1,1-Dimethylcyclopropane

The reaction of mercuric acetate in water solution with 1,1-dimethylcyclopropane was run under the following conditions: the hydrocarbon (25 g) was shaken with a solution of mercuric acetate (110 g) in distilled water (400 ml) at room temperature for 10–12 hours, to nearly complete disappearance of the hydrocarbon layer; the filtered aqueous solution, free of mercuric salts (negative test with alkali), was vacuum-distilled to remove water and acetic acid; the residual oil was dissolved in ether, the solution was again filtered, and the ether was distilled off. The reaction product (3-hydroxy-3-methylbutylmercury acetate, an oil) was dried in a vacuum-desiccator over phosphorus pentoxide; yield 92 g (75%).

The reaction of mercuric acetate (23 g) with 1,1-dimethylcyclopropane (5 g) in methanol solution (80 ml of anhydrous methyl alcohol) and the isolation of the reaction products were done under the same conditions as before. The yield of 3-methoxy-3-methylbutylmercury acetate (oil) was 21 g (82%).

The obtained mercury acetates (in portions of 3 g in 75 ml of water) were converted by treatment with equimolar amounts of potassium chloride, bromide, iodide, cyanide and thiocyanate into the corresponding 3-hydroxy and 3-methoxy-3-methylbutylmercury salts. The reactions were run with stirring and with ice water cooling of the reaction mixture. The acetate of 3-methoxy-3-methylbutylmercury was difficultly soluble in water, and for this reason the potassium salt solutions were added to a water emulsion of the methoxy compound; the reaction mixture was then stirred another 2–3 hours.

The obtained crystalline γ-mercurated alcohols were recrystallized from 40% aqueous alcohol, while their methyl esters were recrystallized from ether. The melting points of these organomercury compounds are given in Table 1.

The thiocyanate and cyanide of 3-hydroxy-3-methylbutylmercury proved to be noncrystallizing viscous oils.

Treatment of 3-hydroxy-3-methylbutylmercury acetate (4 g) with sodium stannite in alkaline solution [2] gave di-(3-hydroxy-3-methylbutyl)-mercury with m.p. 81° (from 40% alcohol); yield 1.7 g (80%).

Found %: Hg 53.67, 53.58. $C_{10}H_{22}O_2Hg$. Calculated %: Hg 53.51.

This compound was obtained in the same yield by a simpler method without isolating the mercury acetate: after conclusion of reaction between the 1,1-dimethylcyclopropane and aqueous mercuric acetate solution the reaction mixture was treated with 20% sodium hydroxide solution until slightly alkaline, filtered, the filtrate treated with an alkaline solution of sodium stannite, and the symmetrization reaction run in the usual manner.

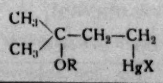
2. Reduction of 3-Hyroxy-3-Methylbutylmercury Chloride By Treatment With Ethylmagnesium Bromide

To an ether solution of ethylmagnesium bromide (prepared from 2.7 g of magnesium and 12 g of ethyl bromide), with water cooling and vigorous mechanical stirring, was added an ether solution (1:5) of 12 g of 3-hydroxy-3-methylbutylmercury chloride. A light-colored oil deposited from the ether solution on conclusion of reaction, being the magnesium bromoalcoholate of the hydroxyalkylmagnesium bromide. The reaction mixture was heated at slight boil for 1.5 hours. The ether layer was decanted, and the oil was washed twice with absolute ether. • Ether was again added to the organomagnesium compound; dilute 2N acetic acid was used for the decomposition.

• The ether solution was treated with water to decompose the organomagnesium compound remaining in it, and then it was filtered; a crystalline precipitate of ethylmercury chloride deposited from the ether layer on standing; m.p. 192°. Literature data: m.p. 192.5° [13]. In addition to the crystalline ethylmercury chloride, the residue after evaporation of all of the ether proved to contain a small amount of diethylmercury, b.p. 55° (14 mm), n_D^{20} 1.5402, the formation of which could have been affected by reaction between the ethylmercury chloride and excess Grignard reagent.

TABLE 1

Crystalline Organomercury Compounds of Structure



OR	X	Name (alkyl-3-methylbutyl)	Melting point	Yield (%)	Remarks
OH	Cl	3-Hydroxyalkylmercury chloride	59—60°	92	Found %: Hg 61.65, 61.81. Calculated %: Hg 62.16
OH	Br	3-Hydroxyalkylmercury bromide	92—93	90	—
OH	I	3-Hydroxyalkylmercury iodide	119—120	80	—
OCH_3	Cl	3-Methoxyalkylmercury chloride	42—43	90	Rapidly deliquesces in the air
OCH_3	Br	3-Methoxyalkylmercury bromide	45—46	85	
OCH_3	CNS	3-Methoxyalkylmercury thiocyanate	37—38	75	
OCH_3	CN	3-Methoxyalkylmercury cyanide	40—41	64	Found %: Hg 60.93, 61.28. Calculated %: Hg 61.18
OCH_3	I	3-Methoxyalkylmercury iodide	—	62	Decomposes in light

The ether layer was separated, and the water layer was extracted with ether. The ether extracts were washed with 40% alkali solution. Removal of the ether by distillation gave 2 g (62%) of tert-amyl alcohol.

B.p. 102–103° (756 mm); n_D^{20} 1.4067; M.p. 3,5-dinitrobenzoate 118°.
Literature [12]: B.p. 102° (756 mm); M.p. 3,5-dinitrobenzoate 117–118°.

A mixture of the obtained 3,5-dinitrobenzoate with the 3,5-dinitrobenzoate from authentic tert-amyl alcohol melted without depression.

3. γ-Mercurated Alcohols and Their Methyl Esters From Methylcyclopropane

To a solution of 159 g of mercuric acetate in 100 ml of distilled water, cooled to -15°, was added 28 g of condensed methylcyclopropane. Then the reaction mixture was shaken for 20 hours on a mechanical shaker. The reaction product (3-hydroxybutylmercury acetate; an oil, soluble in ether and acetone) was isolated in the manner described above.

Methylcyclopropane (28 g) was added to a solution of mercuric acetate (0.5 mole) in 100 ml of anhydrous methyl alcohol, cooled to -50°. On conclusion of reaction, run under the above described conditions, the methyl alcohol and acetic acid were vacuum-distilled at 10 mm. The obtained oil (138 g, 80%) was dried in a vacuum-desiccator over calcium chloride.

3-Methoxybutylmercury acetate is soluble in alcohol, ether and acetone, and difficultly soluble in water.

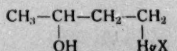
The acetate group in the obtained mercury acetates was replaced by the chloro, bromo, iodo, cyano, and thiocyanato groups by treatment with the corresponding potassium salts.

All of the 3-methoxybutylmercury salts proved to be noncrystallizing oils. Of the 3-hydroxybutylmercury salts, only the chloride, bromide and thiocyanate proved to be crystalline, which were recrystallized from alcohol; the yields, melting points and mercury analyses for the obtained crystalline organomercury compounds are presented in Table 2.

The Symmetrization of 3-hydroxybutylmercury acetate (33.2 g) by treatment with sodium stannite in alka-

TABLE 2

Organomercury Compounds of Structure



X	Name	Melting point	Yield (%)	Hg (%) found	Hg (%) calculated
Cl	3-Hydroxybutylmercury chloride	95—96°	85	64.30	64.88
Br	3-Hydroxybutylmercury bromide	114—115	80	56.12	56.73
CNS	3-Hydroxybutylmercury thiocyanate	65—66	85	59.62	59.08

line solution was run under the usual conditions [2]. The obtained precipitate was filtered; the filtrate was extracted with ether, while the precipitate was washed with acetone. The ether and acetone solutions were dried over sodium sulfate. Removal of the solvents by distillation left a viscous oil, which was vacuum-distilled in a stream of nitrogen; soluble in ether and acetone. Yield 14.7 g (85%).

B.p. 174–176° (12 mm), n_D^{20} 1.5461.

Reduction. The 3-hydroxybutylmercury chloride was reduced by treatment with ethylmagnesium bromide. The reaction products were: sec-butyl alcohol (yield 65%; b.p. 100–101° at 747 mm; m.p. of 3,5-dinitrobenzoate 75–76°), ethylmercury chloride (m.p. 192°) and a small amount of diethylmercury (b.p. 55–56° at 14 mm; n_D^{20} 1.5410).

Literature for sec-butyl alcohol [14]: b.p. 101–102° (750 mm); m.p. of 3,5-dinitrobenzoate 76°.

The mixture of the obtained 3,5-dinitrobenzoate with the 3,5-dinitrobenzoate from authentic sec-butyl alcohol melted without depression.

SUMMARY

1. The reaction of mercuric acetate in water and methanol solutions with 1,1-dimethylcyclopropane leads to cleavage of the three-membered ring and the formation of the 3-hydroxy- and 3-methoxy-3-methylbutylmercury acetates.

2. The same reaction with methylcyclopropane yields the 3-hydroxy- and 3-methoxybutylmercury acetates.

3. Exchange reaction of the obtained acetates with KCl, KBr, KI, KCN and KCNS gave the corresponding (previously unknown) 3-hydroxy- and 3-methoxyalkylmercury salts (where: alkyl = 3-methylbutyl and butyl); the di-(3-hydroxy-3-methylbutyl)-mercury and di-(3-hydroxybutyl)-mercury are also new.

4. The structure of the obtained organomercury compounds (and consequently the location of ring cleavage) was shown by their reduction to the alcohols (replacement of the HgCl group by hydrogen) by successive treatment with ethylmagnesium bromide and water.

5. It was established that the three-membered ring is opened between the alkylated and nonalkylated carbon atoms of the ring.

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CHEMISTRY OF CUPRAMMONIUM SOLUTIONS OF CELLULOSE

VII. THE REACTION OF POLYHYDROXY COMPOUNDS WITH THE AMMINE COMPLEX OF COPPER

S. N. Danilov and M. G. Okun

The widespread theories [2, 3] that compounds of definite composition are contained in cuprammonium solutions of cellulose, where the tetramminocopper cation and individual copper atoms enter the cellulose molecule, replacing the hydrogen atoms in its hydroxyl groups on the type of an alcoholate, must be acknowledged as lacking in proof [1]. These opinions were developed by K. Hess [3] on the basis of the literature data pertaining to the copper-sodium compounds of glycerol [4], and to the ethylenediamine compounds of this trihydric alcohol and higher polyhydric alcohols [2]. The sodium-alkali compounds of glycerol and the alkali-copper compounds of tartaric acid were separated as crystalline precipitates from aqueous-alkali solutions by the use of alcohol [2, 4]. It is possible that the structure of the cuprammonium compounds of cellulose is identical with the structure of the just mentioned substances, but here it is also impossible to consider the composition and structure of the latter as having received unequivocal elucidation. Some authors [5, 6] assign to the cuprammonium derivative of ethylene glycol and other multihydric alcohols an alcoholato-complex nature with necessary involvement of two hydroxyl groups standing in a row.

Normann [7] obtained dark blue precipitates when he treated cuprammonium solutions of cellulose with alkali. Hess and Messmer [8] asserted that the precipitates of Normann have a constant composition and assigned the formulas $[(C_6H_8O_6)_2Cu]Na_2$ and $(C_6H_7O_5Cu)Na$ to the compounds, in which the hydrate water was not taken into consideration. Lieser [9] assigned the composition $2C_6H_{10}O_5 \cdot 1.5Cu(OH)_2$ to the cuprammonium compounds of cellulose on the basis of the analyses of the dark blue precipitates obtained by him when methanol was added to cuprammonium solutions of cellulose. Lieser believes that not all of the hydroxyl groups in cellulose are fully substituted by copper due to the somewhat peculiar micelle structure of cellulose. It is indicated in the literature [10] that water-insoluble compounds are obtained for cellulose and other water-insoluble carbohydrates.

For the purpose of studying the composition of the cuprammonium compounds of cellulose we used in our experiments the method of precipitating the cellulose with alkalis and salts. To be sure, here the danger exists that the original composition of the compounds changes in the precipitation from solutions, especially if the equilibrium character of the reaction for the formation of ammine complexes of copper [11], and apparently also of the cellulose-copper compound, is taken into consideration.

The ratio between the copper and the cellulose in the precipitates studied by the earlier authors (Normann, Traube, Hess, Lieser) varied from 1:1 to 3:2, in which connection it was difficult to avoid mechanical retention of part of the solution by the precipitates; the solution composition was determined by the difference in composition before and after precipitation.

In our experiments the precipitates were analyzed directly, in which connection the excess of solution was separated from the precipitate by more or less uniformly brief, but strong centrifuging.

The isolation of the precipitate is accompanied by decomposition of the solution. The addition of large amounts of alkali produces a reduction in the degree of amination of the cuprammonium base, equilibrium in the solution is disturbed, and cellulose deposits in the precipitate, up to a certain moment containing the compounds of copper and sodium hydroxide, and also ammonia. The analyses, given in the tables, reveal that the ratio of the gram-moles of cellulose and gram-atoms of copper in the precipitates varies around 1:1, the same

as for Hess and Messmer, but it deviates substantially in both directions.

Large excesses of sodium hydroxide in the precipitates are not unexpected when alkalis are used for the precipitation. The use of a large excess of sodium hydroxide solution permits almost complete removal of the copper ion and ammonia, in which connection we have alkali cellulose in the precipitate, the composition of which approaches the ratio $C_6H_{10}O_5 : NaOH = 2:1$. The composition of the precipitates obtained by Normann can be expressed by the formula: $[(C_6H_{10}O_5)_x \cdot yCu(OH)_2 \cdot zNaOH \cdot qH_2O]_n$, analogous to the composition of alkali cellulose: $[(C_6H_{10}O_5)_x \cdot yNaOH \cdot zH_2O]_n$.

Cellulose, being a powerful adsorbent, retains the indicated components within certain, but to be sure extremely variable, ratios. Even if the cellulose was to form chemical compounds with them through primary valences, constant compositions for the compounds would be highly improbable due to the high molecular weight of cellulose, even in the dissolved state.

The use of ammonium sulfate as a precipitant leads to a rapid shifting of the equilibrium, in which connection an excess of this precipitant results in the separation of nearly pure cellulose. When lithium chloride is used as precipitant a certain amount of LiOH is contained in the precipitates.

The coagulative action of various alkalis and salts on cuprammonium solutions of cellulose was studied earlier in our laboratory [12].

When small amounts (up to 1%) of sodium hydroxide are added an increase in cellulose solubility is observed with a reduction in the limiting amounts of copper hydroxide needed to dissolve the taken cellulose sample. This was also known earlier [13] and only confirmed by us here, but still it is impossible to agree with Hess' opinion [3] that this is specifically due to replacement of cationic copper by sodium hydroxide with separation of the cuprammonium complex. It is obvious that alkali at low concentrations increases the swelling of cellulose. A study of the precipitates can give some indication as to their composition, but it fails to reveal the chemical nature of the interrelationships between the components, all the more so since the ratios between them are not constant. We postulated that the experiments described by us below on the spectrometric study of cuprammonium solutions could reveal the alcoholate nature of the compounds, provided it was present. However, the light absorption curves fail to support the hypotheses of Hess and Traube.

The spectrometric method [14, 15] has been used to study the ammine and ethylenediamine complexes of copper and the cuprammonium solutions of polyhydroxy compounds.

With this method, M. I. Arkhipov [16] found that the cuprammonium compound of cellulose is more highly aminated than the cuprammonium base. He postulated that the compound between cellulose and the ammine complex is formed through the hydrogen bonds of the reacting substances, i.e., it has the properties of a molecular compound.

Our spectrographic studies of the cuprammonium reagent, the cellulose film itself, and the cuprammonium solution of cellulose, revealed that the optical density curves of the cuprammonium reagent and cuprammonium solution of cellulose have the same shape and differ at a given wavelength only by the light absorption value of cellulose. These experiments also give basis to state that possibly molecular compounds are formed between cellulose, glucose, oxycellulose, cellulose ethers and the copper ammine complex, but not compounds that are based on the primary valences, for example, of the alcoholate type. We came to the same conclusion in our previous paper [1] on the basis of electrophoresis experiments [17], and with ion exchangers.

It is known that Rosenblatt [18], using optical methods, found that reaction of cupriethylenediamine with glycerol gives a compound that contains only cationic copper.

The phenomenon of swelling plays the major role when cellulose is dissolved in Schweizer reagent. It is possible to postulate that the composition of the cuprammonium compounds of cellulose is expressed by the formula of the molecular compound: $\{(C_6H_{10}O_5)_x \cdot [Cu(NH_3)_m(OH)_2]_y \cdot (H_2O)_z\}_n$.

Other, even more delicate and reliable investigation methods are needed, which could help in deciphering the component interrelationships that exist in cuprammonium solutions of cellulose.

EXPERIMENTAL

We will discuss the composition of the precipitates that are formed when cuprammonium solutions of cell-

ulose are treated with solutions of alkalis and salts, and also the spectrophotometric characterization of Schweizer's reagent and the cuprammonium solutions of cellulose and various other polyhydroxy compounds.

One batch of cotton cellulose was used with the following characteristics: α-cellulose 98%, copper number 0.3, ash 0.3%, moisture 5%.

To avoid contamination by foreign electrolytes the Pel_got method [19] was used to prepare a well-washed moist crystalline copper hydroxide. In the rayon literature the crystalline copper hydroxide is incorrectly named Furness (American firm) salt, and at times as Habermann salt [20]. Each batch of salt was analyzed (electrolytically) for its copper content. To prepare this salt a 25% ammonia solution, taken in 29% amount on the weight of copper sulfate pentahydrate, was added to a solution of copper sulfate (in 4.5 parts of water), and the whole was diluted with water to 21 volumes on the weight of copper sulfate. Then 10% sodium hydroxide solution, taken in 32.1% amount on the weight of copper sulfate pentahydrate, was added with stirring, in which connection a light-blue crystalline precipitate of copper hydroxide was obtained.

The cuprammonium solutions of the polyhydroxyl compounds were obtained by the "blue mass" method under the earlier described conditions [1], in which connection the solutions were prepared separately for each experiment and were kept for a day.

In dissolving the polyhydroxyl compounds, a constant excess ammonia concentration of 15% on the weight of solution was used so as to avoid variation in the properties of the solution as a function of the amount of ammonia.

To determine the solubility of the polyhydroxy compounds several solutions of the same concentration of polyhydroxy compound and variable concentration in copper were prepared. The minimum and sufficient copper concentration, necessary to obtain solution, was found, in which connection the absence of undissolved particles was checked under the microscope.

As a result, the optimum ratios between the copper (in gram-atoms) and the polyhydroxyl compound (in gram-moles) were established. The ratio between copper and such a polyhydroxyl compound as cellulose is determined by the amount of cellulose per unit of solution volume: the higher the concentration in cellulose, the lower the ratio, as is known, between the amount of copper needed for solution and the amount of cellulose.

1. Ratio of the Components in Cellulose-Cuprammonium Precipitates

To elucidate the nature of cuprammonium solutions of cellulose a large number of experiments were run on the isolation and study of the composition of the precipitates obtained in the action of the precipitants. The literature data on the "Normann precipitates" gave hope of obtaining precipitates with more or less constant properties in accord with the equilibrium reactions for the formation of copper ammine complexes and the products of their reaction with cellulose. It is understood that due to the high-molecular nature of cellulose, the complexity of its interrelationships with the other components in the solution, and the incomplete "coppering" of its hydroxyl groups, an indication as to whether alcoholate derivatives are actually formed, could be expected even in the case of obtaining only a number of average values in the analyses. We determined the composition of the precipitates obtained in the addition of various concentrations of alkali, ammonium sulfate and lithium chloride solutions. The caustic was chosen in connection with the known method of obtaining the "Normann precipitates", while the indicated salts were chosen due to their coagulative action [12] on cuprammonium solutions of cellulose.

The precipitates were obtained and their composition determined as follows. To a 4% (based on cellulose) cuprammonium solution of cellulose, containing 2.5% copper (ratio $\frac{\text{gram-atom Cu}}{\text{mole cellulose}} = 1.6$) and 15% ammonia in 100 g of solution, was added a solution of the precipitant, the mixture shaken on a shaker for 2–3 hours, and then it was left to stand for 12 hours. The precipitate was separated from excess solution by centrifuging for a period of twenty minutes at 2000 r.p.m. Centrifuging for a longer time leads to decomposition of the precipitate due to excessive removal of ammonia.

The obtained precipitate was analyzed for cellulose, copper, and sodium or lithium, for which 50 g portions of the solution were taken, and two parallel experiments were run.

To obtain a more valid average value, the determination of each component in the given precipitate was repeated 5 times, in which connection a separate sample of the precipitate was taken for each component part

of the solution. Cellulose was determined in the precipitate by the wet combustion method using a mixture of potassium bichromate and sulfuric acid, with subsequent and previous titration with sodium thiosulfate, while copper was determined electrolytically.

To determine copper a small amount of water was added to a known weight of the precipitate, and the precipitate was comminuted with a glass rod; then the mixture was acidified with dilute sulfuric acid, after which concentrated sulfuric acid was added to hydrolyze the cellulose, so that the latter, depositing from solution as small clods, would not interfere with the analysis. The addition of concentrated acid directly to the precipitate caused it to turn brown and made electrolysis difficult. Sodium and lithium were determined in the alkalis by titration with 0.1N sulfuric acid, in which connection to remove ammonia the sample was first heated in water until it boiled. The alkali or salt was added to the cuprammonium solution in such amount that all of the cellulose went into the precipitate, which simplified determination of the components in the precipitate.

Depending on the nature of the precipitant the precipitates differed in external appearance. The addition of alkali caused the whole solution to turn into a gelatinous mass, nearly filling the whole vessel. When shaken and stored, the mass decomposed into individual gel-like clods, containing the cuprammonium reagent, and here less blue than the original, due to ammonia loss; the liquid was centrifuged from the precipitate as completely as possible. When the precipitate was dried in vacuo, its components – cellulose, copper hydroxide and sodium hydroxide – separated individually. When dried in the air, the precipitate decomposed with the separation of black copper oxide.

The salts precipitated the precipitates from the cuprammonium solution as small scales, which easily passed through the openings during centrifuging. It became necessary to put asbestos fiber, moistened with aqueous salt solution, on the bottom of the tubes in the centrifuge.

We were unable to obtain precipitates from the cuprammonium solutions of oxycellulose, methylcellulose and hydroxyethylcellulose, since here the precipitates glued together easily and centrifuged with difficulty.

In order not to take up space for tables on the analysis of the numerous precipitates obtained in the precipitation with sodium hydroxide, we present a summary table, in which we show only the change in the ratio of the components in the precipitates as a function of the amount of added alkali (Table 1). The amount of components in the obtained precipitates varied from ± 1 to $\pm 5\%$.

The number of moles of sodium hydroxide per mole of cellulose in the precipitates was inordinately large and goes beyond the limits of stoichiometric proportions, which was conditioned by the excess of sodium hydroxide, taken as precipitant. With larger amounts of precipitant the amount of copper in the precipitate decreased.

If attention is turned to the ratio of gram-moles of cellulose and gram-atoms of copper, then in this case it can only tentatively be said that it approaches the ratio 1:1.

TABLE 1

Expt. nos.	Amount of NaOH added (%)	Ratio of components in precipitate in		
		$C_6H_{10}O_5$ (g-mole)	Cu (g-atom)	Na (g-atom)
1	1.82	1	1.35	6.2
2	3.33	1	1.52	6.7
3	5.70	1	1.06	12.8
4	6.67	1	1.27	17.3
5	7.50	1	1.27	16.4
6	8.0	1	0.96	15.3
7	11.41	1	1.04	14.5
8	10.0	1	1.05	15.7
9	12.3	1	1.12	14.5

Similar results were also obtained in the case where lithium chloride was used as the precipitant. In the precipitates that were obtained when ammonium sulfate was the precipitant the ratios between the cellulose and copper were extremely variable, since this salt readily elutes copper hydroxide from the precipitate. Consequently, to obtain precipitates with ammonium sulfate, it is completely unsuitable to use an excess of it. If very large amounts of precipitant – sodium hydroxide – are taken, then the copper and ammonia are washed out completely. Cellulose, sodium hydroxide and a very small amount of copper hydroxide remained in the precipitate that had been washed with 4% sodium hydroxide solution, and then with anhydrous ethyl alcohol. It might be mentioned that the precipitate in these cases proved to have an alkali cellulose composition close to the usual composition, which can be seen from Table 2 ($C_6H_{10}O_5$: NaOH ratio about 2:1).

TABLE 2

Alkali content in %	Amount of cellulose in g	Amount of alkali in g	Ratio (in g-moles)	
			$C_6H_{10}O_5$	NaOH
10	1.78	0.22	2	1
10	1.89	0.22	2	0.94
3.3	1.85	0.23	2	0.97

As a result, precipitates are formed when cuprammonium solutions of cellulose are treated with a sufficient quantity of sodium hydroxide, in which the copper hydroxide is gradually replaced by sodium hydroxide, right up to the formation of alkali cellulose.

It should also be indicated, without giving figures, that if the alkali is added in small amounts (from 0.3 to 1% on the solution weight) to the "blue mass" in the preparation of the solution, then the solubility of the cellulose increases and the amount of copper hydroxide, necessary to dissolve a given amount of cellulose, decreases. The cellulose fails to dissolve when more than 1% of alkali is added, and when 1.2% of alkali is added a precipitate deposits in the finished cuprammonium solution of cellulose.

Two series of experiments were run: at a constant cellulose and copper concentration, and at a constant copper and alkali concentration. For example, 1% cellulose, 1.2% copper, 0.3–1.2% alkali and 15% ammonia.

Such a favorable influence of small amounts of alkali, far from stoichiometric proportions, also observed earlier in the literature [20], indicates that sodium hydroxide augments the swelling of cellulose as long as it is taken in small amounts, while when taken in excess, it causes precipitation from solution.

2. Spectrographic Studies of Cuprammonium Solutions of Polyhydroxy Compounds

We studied the absorption spectra of the cuprammonium reagent, cuprophane and cellophane films, copper salts, cuprammonium solutions of cellulose, methycellulose, hydroxyethylcellulose, oxycellulose, sucrose, glucose, glycerol, alginic acid, sodium alginate and tartaric acid on an SF-11 spectrophotometer in the visible region from 4000 A to 1 μ, and in the ultraviolet region from 2000 to 4000 A. An incandescent bulb served as the light source for the visible region, and a hydrogen lamp for the ultraviolet region. The recording in the long-wave region was done with an antimony-cesium photoelement, and in the short-wave region with an oxygen-cesium photoelement. The value of the optical density (D) was determined [21], depending linearly on the values of the absorption coefficient, concentration, and thickness of the absorbing layer (d).

Value D was measured in a hermetically covered cuvette with quartz windows. The thickness of the absorbing layer (d) was 0.1 and more frequently 1 and 5 mm. The zero reading was made on the basis of air-absorption. The measurements were made at 5 mμ intervals, and more frequently at 10 mμ intervals. The curves showing the relationship between the density (D) and the wavelength λ (in mμ) were constructed on the basis of the measurement data.

The cuprammonium solutions were prepared as had already been described above. The cellulose cuprophane film for the experiments was obtained directly from a cuprammonium solution of cellulose on a quartz plate. We also determined the optical density of commercial cellophane film after it had been soaked for a long time in water to remove glycerol (plasticizer).

Different samples of oxycellulose were characterized: acid number (27–31 ml of 0.01N sodium hydroxide solution), copper number 10–20, and a carboxyl group content, based on carbon dioxide cleavage (by the method of heating with 12% hydrochloric acid), ranging from 0.7 to 0.9%. The methylcellulose contained 9.8–10.1% OCH_3. The hydroxyethylcellulose had a low degree of substitution and was soluble in water.

First of all we compared the solutions of copper acetate and sulfate with the cuprammonium reagent and with Fehling solution.

The curve for the optical density of a 1% copper acetate solution shows a somewhat diffuse minimum in the 450–510 mμ interval, and at 660 mμ, the solution already absorbs completely. The copper sulfate solution

with a copper concentration of 1% almost completely permits the passage of light in the wide interval of 400–575 mμ. Then the optical density curve for the solution slowly rises, shows an ill-defined maximum at 800 mμ, and after this the optical density of the solution slowly decreases. As a result, in the wavelength region of interest to us (600–650 mμ) a 1% copper sulfate solution is almost completely transparent at a layer thickness of 5 mm. With increase in the copper concentration of these solutions up to 20%, and with the same layer thickness, the absorption of the solution in the 500–650 mμ region rises sharply, and at 660 mμ becomes infinitely great.

The absorption spectra of the cuprammonium reagent were studied at a copper concentration of 1%, which is approximately the maximum amount of copper that can be dissolved in 25% aqueous ammonia solution without leaving a residue. Since characteristic inflections on the optical density curve were hardly evident when the cuprammonium reagent was taken as a thin 0.1 mm layer, which can be seen from Fig. 1, we therefore decided to work with layers having a thickness of 1 and 5 mm. The changes in the spectrum of the cuprammonium solution when various polyhydroxy compounds were added to it were determined in relation to the spectrum of the cuprammonium reagent itself.

The cuprammonium reagent absorbs completely in the ultra-violet region. Only in a very thin 0.1 mm layer was some reduction in density observed in the 235–250 mμ interval. The cuprammonium reagent begins to pass light with a layer thickness of 1 mm at 285 mμ (D 1.7); the optical density drops sharply and reaches a minimum at 420 mμ (D 0.06), and then rises; the curve shows a maximum at 640 mμ (D 1,131). Then the optical density curve of the cuprammonium reagent gradually approaches the abscissa. Consequently, the optical density curve of this solution has two sharply expressed inflections – a minimum at 420 mμ and a maximum at 640 mμ. With a layer thickness of 5 mm the points of inflection correspond to the same wavelengths, but the value of the optical density at wavelength 475–1000 mμ is higher than with a layer thickness of 1 mm (see Fig. 1.).

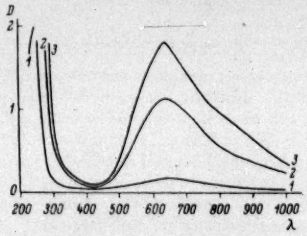

Fig. 1. Optical density of a 1% cuprammonium solution.
Layer thickness: 1) 0.1 mm, 2) 1 mm, 3) 5 mm.

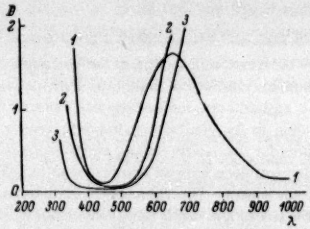

Fig. 2. Optical density of solutions.
1) Fehling solution, 2) copper acetate solution, 3) copper sulfate solution.

As can be seen from Fig. 2, the optical density curve for Fehling solution differs sharply from the optical density curves for the salt solutions, but is similar to the absorption curve for the cuprammonium solution. Fehling solution absorbs completely at 360 mμ and only the minimum and maximum on the curve are shifted somewhat in comparison to the curve for the cuprammonium reagent, namely $\lambda_{min.}$ 440 mμ and $\lambda_{max.}$ 670 mμ. This shows that comparable ratios exist between the components in the cuprammonium reagent and in Fehling solution. It is possible that copper complexes of variable composition are present in both cases.

It is probable that the presence of a carboxyl group in tartaric acid exerts an influence. The optical densities of standard cuprammonium solutions were measured, to which had been added sucrose, glycerol, glucose and tartaric acid in 1% amounts. Without presenting either tables or the corresponding figures, we will only mention the main results with the staatement that chemical reaction between these substances and the cuprammonium comple fails to be such that it could be detected on the optical density curves.

Water solutions of the investigated low-molecular substances begin to pass light at about 320 mμ. The optical density of the solutions drops sharply in the interval 320–340 mμ so that all of these solutions are completely transparent at 450 mμ. The solutions (1%) of sucrose, glycerol and glucose in standard cuprammonium reagent show optical density curves that are almost superimposed on the optical density curves of the cuprammonium reagent itself. The solutions begin to pass light in the interval 320–350 mμ and show an optical density minimum at 420 mμ and maximum at 640 mμ.

In the interval 320–450 mμ the optical density of cuprammonium solutions of glucose and other substances is somewhat greater than the density of the cuprammonium reagent due to the absorption value of the dissolved substance. In the interval 450–1000 mμ, in which these substances are transparent, a complete agreement of the optical density curves for the cuprammonium reagent itself and the solutions of the indicated substances was observed.

The optical density for tartaric acid shows $\lambda_{min.}$ 430 mμ and $\lambda_{max.}$ 640 mμ, but is somewhat greater in magnitude (D 1.964 instead of the 1.820 for the cuprammonium reagent).

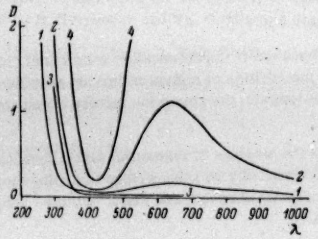

Fig. 3. Optical density curves of cellulose solutions.
1) 0.5% cuprammonium solution of cellulose–layer 0.1 mm, 2) 0.5% cuprammonium solution of cellulose–layer 1mm, 3) $D_{substance} = D_{solution} - D_{solvent}$ ($D_{cellulose}$), 4) 0.8% cuprammonium solution of cellulose–layer 5 mm.

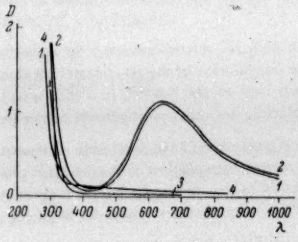

Fig. 4. Optical density curves of cellulose solutions.
1) cuprammonium solution, 2) cuprammonium solution of cellulose, 3) $D_{substance} = D_{solution} - D_{solvent}$ ($D_{cellulose}$), 4) cuprophane film.

The optical density curve of the cuprammonium reagent is changed somewhat by the presence of tartaric acid, apparently due to its carboxyl groups.

We will describe a brief study made of the cuprammonium solutions of cellulose, its ethers, and other polysaccharides.

To determine the changes when cellulose is introduced into the cuprammonium reagent the absorption spectra of cuprophane and cellophane films in the interval 235–1100 mμ were obtained. The cuprophane film (due to traces of copper) is not transparent in the ultraviolet and begins to pass light only at 300 mμ, after which the optical density drops sharply at 300–350 mμ (from 1.8 to 0.14), and then asymptotically approaches the abscissa, i. e., the film is almost completely transparent.

Cellophane film is transparent in the ultraviolet region, but beginning with 350 mμ the optical density curves of the cuprophane and cellophane films almost completely coincide.

The cuprammonium solutions of cellulose were measured at concentrations of 0.5 and 0.8%, with layer thicknesses of 0.1–1 and 5 mm. It was found that at a thickness of 0.1 mm the characteristic inflections on the optical density curves become smoother and more diffuse, while with a layer thickness of 5 mm the solution absorbs completely even at 520 mμ; consequently, the most suitable layer thickness is 1 mm.

The optical density curve for the cuprammonium solution of cellulose was compared with the same curve for the cuprammonium reagent itself, both having the same copper and ammonia concentrations. It was found that the density curves of these solutions coincide, having an optical density minimum at 420 mμ and a maximum at 640 mμ.

In the interval 300–350 mμ the optical density of the cellulose solution is somewhat greater than that of the standard solution.

The difference between these densities, calculated by the formula $D_{substance} = D_{solution} - D_{solvent}$, is identical with the optical density of the cuprophane film. The optical density curves coincide completely at 500–100 mμ. The optical density curves for the cellulose solutions are shown in Figs. 3 and 4.

In the limits 200–1000 mμ and a layer thickness of 1 mm, the curves for 0.5% cuprammonium solutions of oxycellulose, alginic acid and sodium alginate practically coincided among themselves. The curves for methylcellulose and hydroxyethylcellulose, being nearly superimposed, one over the other, were also of a similar nature. Here in all cases, the optical absorption minimum was at 420mμ, and the maximum at 640 mμ, the same as for the cuprammonium reagent itself.

SUMMARY

1. To study the interrelationships between the components in cuprammonium solutions of cellulose, we studied the composition of the precipitates obtained in the addition of sodium hydroxide or lithium chloride to the solutions, and we also studied, in a wide wavelength interval, the absorption spectra of cuprammonium solutions of cellulose and other polyhydroxyl compounds.

2. The precipitates have a variable composition in the presence of substantial alkali concentrations, in which connection the cellulose to copper ratio can only tentatively be acknowledged as being close to 1:1. In the presence of excess alkali, the copper reagent is completely removed, and alkali cellulose remains, the composition of which approximates the ratio $2C_6H_{10}O_5:1NaOH$.

The precipitates fail to show the stoichiometric proportions that are indicated in the literature for the Normann compounds.

3. The spectrophotometric studies reveal that the absorption spectra of the cuprammonium reagent and of Fehling solution are essentially different from the spectra of copper acetate and copper sulfate, which indicates the characteristic chemical relationships between the components in these solutions.

4. The spectra of the cuprammonium solutions of cellulose and other low- and high-molecular polyhydroxy compounds fail to differ from the absorption spectrum of the cuprammonium reagent (Schweizer reagent) itself, which does not support the presence of individual characteristic compounds between ammine complexes and cellulose.

Consequently, colloidal-chemical phenomena take place when cellulose is dissolved in Schweizer reagent with the possible formation of very unstable molecular compounds between the cellulose and the copper ammine complexes.

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ROLE OF PHOSPHORIC ACID IN THE STUDY AND TREATMENT OF CELLULOSE

I. THE SWELLING AND SOLUTION OF CELLULOSE IN PHOSPHORIC ACID

S. N. Danilov and N. F. Gintse

Phosphoric acid, readily dissolving cellulose and slowly hydrolyzing it, can have great, already noted, significance in the study and treatment of cellulose.

We find the first mention of the use of phosphoric ("sirupy") acid as an agent capable of producing swelling, contraction, and then solution of the cellulose fiber in the studies of Mercer, and later in the studies of Hübner and Pope [1].

Phosphoric acid was not used in the numerous studies made by Girard [2] on the preparation and study of hydrocellulose preparations. It was used for the preparation of hydrocellulose ("dextrins") later [3], in which connection the weak hydrolyzing action exerted by phosphoric acid on cellulose was noted, as was also the high viscosity of cellulose solutions in concentrated phosphoric acid. Then Karrer and Lieser [4] prepared an alkali-soluble hydrocellulose (in 8% sodium hydroxide) by the precipitation of cotton cellulose from its solution in 84% phosphoric acid, which was characterized by a low copper number, i. e., by a low degree of degradation.

With phosphoric-nitric acid mixtures fully substituted cellulose nitrates [5, 6] with a maximum retention of the size of the cellulose molecules [7] were obtained, in which connection phosphoric acid, in contrast to sulfuric acid, does not form mixed nitrate esters during nitration.

Having observed the exceedingly small destructive action exerted by phosphoric acid on cellulose and the nonoxidizability by air of phosphoric acid solutions of cellulose, Ekenstam proposed the use of concentrated phosphoric acid as a solvent for cellulose in the determination of its molecular weight [8], and also for the fractionation of cellulose [9].

Concentrated phosphoric acid is also used in the microscopic study of cellulose fibers as a swelling agent in their defibrillation [10]. In Staudinger's experiments [11] on the precipitation of hydro- and oxycellulose preparations from strong phosphoric acid, the degree of polymerization shown by the cellulose as the result of precipitation (immersion in 89–90% phosphoric acid for 12 hours at 0°) proved to be unchanged.

After the studies of Ekenstam, devoted to a study of the properties of cellulose solutions in mineral acids of high concentration, including phosphoric acid, in which connection the phenomenon of the swelling of cotton fiber in various concentrations (73–90%) of phosphoric acid was also studied, there failed to be any further systematic study made in this field.

In this communication we studied the influence of various conditions (concentration of acid and cellulose, nature of the cellulosic material and method of solution) on the solubility of cellulose in various concentrations of phosphoric acid and the influence of temperature and time of solution on the degree of hydrolysis shown by the cellulose regenerated from the solution.

EXPERIMENTAL

1. Solubility of Cotton Cellulose in Various Concentrations of Phosphoric Acid.

To eliminate the possible influence of a high viscosity, characteristic for phosphoric acid solutions of cellulose, on the solubility value, the determinations were run in highly dilute solutions. A 0.500 g sample of air-dry bleached linters with a known moisture content (about 5%) was stirred with 450 ml of phosphoric acid. At first, the acid was added in small portions, with thorough stirring with a glass rod; after all the acid had been added the mixing was continued on a mechanical "shaker" for 2 hours. This amount of time was sufficient for complete solution without the acid exerting a noticeable hydrolytic effect on the cellulose. Then the solution was filtered through a weighed glass filter; the residue on the filter was first washed with the same concentration of acid as was used to dissolve the taken sample, then with water until neutral, dried on the filter at 105° to constant weight, and weighed. The solubility was calculated in percent of the amount of dry fiber in the starting sample. In the cases where the sample dissolved completely (checked under the microscope) the solution was not worked up, and the solubility was taken as equal to 100%.

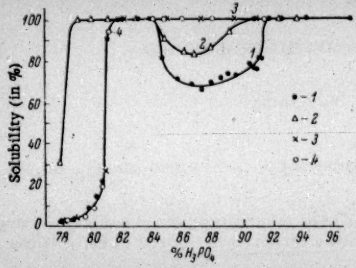

Fig. 1. Solubility of linters and sulfite cellulose in various concentrations of phosphoric acid. 1) solubility of the linters directly in the acid, 2) solubility of sulfite cellulose directly in the acid, 3) solubility of linters after swelling in water, 4) solubility of linters after swelling in 73% acid.

Our data (Curve 1 in Fig. 1) show that it is possible to dissolve cotton cellulose in two different concentration intervals of strong phosphoric acid, not only at 82–84%, as Ekenstam indicated, but also at 92–97%. More concentrated acid was not used, since it is obtained with difficulty in noncrystalline form at room temperature. Only partial solution occurs at intermediate concentrations (84–92%) of the acid. It is characteristic that the region of complete solution corresponds to those concentrations of acid at which it exists in the form of hydrates: the monohydrate – $H_3PO \cdot H_2O$ (84.4% acid) and the polyhydrate – $2H_3PO_4 \cdot H_2O$ (91.6% acid), which apparently is the reason for the stronger solvent action shown by the acid in these concentration limits. The obtained data can serve as additional proof of the role played by hydrates in dissolving cellulose in concentrated electrolyte solutions. Studying the vapor pressure and composition of nitric acid in phosphoric-nitric acid mixtures, Danilov and Matveev [6] found that a relationship existed between the vapor pressure of nitric acid and the presence of the specifically indicated hydrates of phosphoric acid.

2. Solubility of Sulfite Cellulose in Various Concentrations of Phosphoric Acid.

Ekenstam [8] studied the solubility of cellulose samples with different degrees of polymerization (DP) in 73–83% phosphoric acid, i. e., in the region of the first ascending branch on our curve. To verify the influence of the DP of cellulosic material over the expanse of the whole curve, we ran a series of experiments, similar to the preceding, with sulfite viscose cellulose. The latter was used in the form of a well-crumbled air-dry paper mass. As the obtained data show (Curve 2 in Fig. 1), with decrease in DP of cellulosic material both regions of unlimited swelling on the solubility curve increase, in which connection their increase proceeds in both cases toward lower concentrations. The intermediate region of incomplete solubility is correspondingly abridged, in which connection the solubility of the cellulosic material increases in absolute value.

3. Influence of the Method of Solution on the Solubility of Cellulose in Various Concentrations of Phosphoric Acid.

As is known, phosphoric acid solutions of cellulose, serving for viscosimetric determinations, are prepared by previous swelling of the cellulose in water or more dilute acid. In a number of variations, the final phosphoric acid concentration in this connection goes beyond those limits, in which, according to the former data of Ekenstam, and also according to our new data, it is possible to obtain complete solution of the cellulose when it is reacted directly with the acid. To delineate the role played by preliminary swelling, we determined the solubility of cellulose in various concentrations of phosphoric acid after its preliminary swelling in water and 73% phosphoric acid.

a) Solubility of Cellulose in Various Concentrations of Phosphoric Acid After Preliminary Swelling in Water.

A 0.500 g sample of air-dry bleached linters with a known moisture content was soaked in 50 ml of water. After 1 hour, 400 ml of the desired concentration of strong acid was added. To avoid heating up, the acid was added gradually in drops in 1 hour (this variation of the treatment reproduces the directions of Stamm and Cohen [12]); then additional mixing was maintained for an hour. On conclusion of solution, the concentration of acid in the solution was determined in the filtrate after the amount of undissolved cellulose had been determined. Further determinations were made the same as in previous experiments.

The obtained data (Curve 3 in Fig. 1) show that the preliminary swelling in water does actually assure subsequent solution of the cellulose in any concentration of acid above 82%. The intermediate region of incomplete solution, characteristic for the preceding curves, vanishes. There is no change in the solubility of cellulose in the acid concentration range from 78 to 82%.

b) Solubility of Cellulose in Phosphoric Acid After Preliminary Swelling in 73% Phosphoric Acid.

This variation of preliminary swelling was adopted in the viscosimetric method of Ekenstam. A 0.500 g sample of air-dry bleached linters was covered with 250 ml of 73% phosphoric acid and let stand for 1.52 hours. Then 200 ml of strong acid was gradually added (heating up was not observed), and mixing was continued for 1.5 hours with mechanical shaking. The treatment of the solutions and determination of the solubility were run the same as in previous experiments. As we can see, the obtained data (Curve 4 in Fig. 1) completely coincide with the data of the preceding experiment.

As a result, independent of whether it was done in water or in 73% phosphoric acid, the introduction of preliminary swelling makes it possible to assure complete solution of the cellulose over the whole curve, beginning with an acid concentration of 82%. There fail to be any changes in the cellulose solubility on the ascending portion of the curve (acid concentration 78–82%). From this, it follows that the role played by preliminary swelling in the preparation of phosphoric acid solutions of cellulose reduces only to the fact that we achieve the possibility of preparing these solutions by the method of gradually increasing the strength of the dissolving acid. Specifically, in all cases we pass through the first region of unlimited swelling. Further increase in the acid concentration cannot limit the already achieved complete solution. For this reason, the use of preliminary swelling is an expedient means of preparing phosphoric acid solutions of cellulose. For this it is better to use acid, and not water, so as to avoid heating up in the subsequent addition of concentrated acid.

Incidentally, we will mention here that the obtained data do not agree with the statements made by Stamm and Cohen [12] that in general cotton cellulose cannot be dissolved by its direct treatment with strong phosphoric acid. Evidently, in this connection, Stamm and Cohen employed an acid whose concentration was outside the limits of both regions of unlimited swelling (they do not indicate the acid concentration). This is all the more probable for the reason that in all of their other viscosimetric determinations they used acid with a concentration of 86–92%. However, it is also possible that the authors based their conclusion on the difficulty of solution shown by cotton cellulose with high DP.

4. Influence of the Cellulose Concentration on its Solubility in Strong Phosphoric Acid.

These experiments were run for the purpose of elucidating the conditions needed to obtain homogeneous solutions of cellulose in strong phosphoric acid with a sufficiently high cellulose content in them, suitable for the technical utilization of these solutions.

Samples of bleached air-dry linters were crushed in mortars for 1 hour with sufficient amounts of 84% phosphoric acid to respectively give 2, 3, 4, 5 and 7.5% solutions, after which the samples were allowed to stand in beakers, covered with polished glass plates, at room temperature. The degree of solution (checked under the microscope) was determined at definite time intervals.

Immediately after mixing the cellulose and acid, thick gelatinous masses with solitary undissolved fibers were obtained for the samples containing 2–4% cellulose and with a large amount of undissolved fiber for the samples with a 5–7.5% cellulose content. The consistency of the mass changed in measure with standing. After 12-hour standing, the sample with 2% cellulose was converted into a viscous, transparent, visually empty sirup. The sample with 3% cellulose was converted into the same type of sirup after 24 hours, and with 4% cellulose

on the fourth day, while the sample with 5% cellulose was converted into a sirup after 5 days, but it still retained solitary undissolved fibers. In the sample with 7.5% cellulose, changing into a sirup only after 20 days, the amount of undissolved fibers failed to change during the whole standing time. For the samples with a cellulose content of 2–4%, in measure with their standing, it was possible to observe under the microscope the gradual dissolving of the fiber: at first changes in the contours, then dismemberment into little chains and links, and finally complete disappearance. In the sample with 7.5% cellulose, even after a month, it was possible to find nearly unchanged, unswollen, but distorted fibers with undamaged contours and a clearly visible canal. A slow and incomplete solution of the samples with a higher cellulose content depends on the exceedingly high viscosity shown by such masses, making it difficult for the acid to get to the individual fibrils, already enveloped by a viscous solution layer.

The use of a two-phase dissolving method (i.e., preliminary swelling in 73% acid, followed by squeezing and the addition of strong acid) failed to show any advantages. However, at the start of mixing the mass was somewhat more readily homogenized, became clear more rapidly, and was more sticky, but for the rest we failed to observe any difference between the samples prepared by the two-phase method and the one-phase method. The content of individual undissolved fibers was approximately the same in both of them. In both cases the high viscosity of the mass served as the same hindrance for their solution.

However, the picture underwent a change if we made use of heat in order to obtain solution. If in 1 hour after the start of mixing the cellulose and acid a sample was heated at 30, 40 or 50° for a short time (30 minutes–1 hour), then it was easily transformed into a mobile sirup, failing to show any indications of undissolved fibers or of their portions. The higher the cellulose concentration in the sample, the longer or the higher the heating temperature needed to convert it into a sirup. With the aid of heat it was possible to attain complete solution even for the mass with a 7% cellulose content.

The use of reduced temperatures (0 and –11°) in the dissolving failed to give any advantages with respect to the rate and completeness of solution.

5. Influence of the Time of Storage of the Solutions and of the Solution Temperature on the Properties of Regenerated Cellulose.

Since it proved possible to obtain concentrated solutions of cellulose in phosphoric acid only under the conditions of prolonged treatment or the use of heat, it seemed expedient to elucidate to what extent these operations affected the keeping properties of cellulosic material.

In Figs. 2 and 3 we present the data on the characterization of some hydrocellulose preparations that had been isolated from a 4% solution of linters in 84% phosphoric acid, which had been heated at 40 and 50° for 1 hour, or had been allowed to stand for a long time. The hydrocellulose was isolated from the solutions by precipitation with ice water. As can be seen from these plots, the cellulose showed comparatively little degradation when its phosphoric acid solutions were allowed to stand or when they were heated for a short time, provided the time of standing did not exceed one day, or the heating temperature 30–35°. Consequently, the possibility is not excluded of using moderate heating or the prolonged treatment of the cellulosic material with acid in the preparation of technical solutions of cellulose in phosphoric acid. In their properties the hydrocelluloses, isolated from phosphoric acid solutions of linters that had been subjected to heating for 1 hour at 40–50° or had been allowed to stand at room temperature for 4–6 days, are close to the ordinary technical cellulose hydrates, for example rayon.

When the solutions are heated for 1 hour at 30° the keeping properties of cellulosic material are impaired to approximately the same degree as when the solutions are allowed to stand for a day; when heated for 1 hour at 40° – to the same extent as when allowed to stand for 3 days, and when heated to 45° – to the same extent as when allowed to stand for six days.

SUMMARY

1. The curve for the solubility of cellulose in strong phosphoric acid as a function of the concentration of the latter shows two maxima (the second without a descending branch), corresponding to the regions of unlimited swelling with an intermediate region of incomplete solution between them.

2. Both of the regions for the unlimited swelling of cotton cellulose are located in those concentration in-

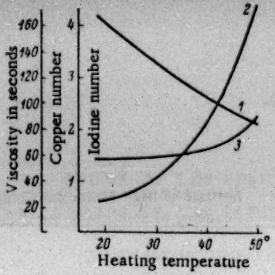

Fig. 2. Influence of heating the solutions on the properties of regenerated cellulose.
1) viscosity, 2) copper number, 3) iodine number.

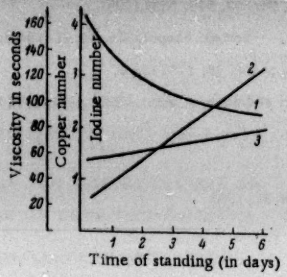

Fig. 3. Influence of standing of the solutions on the properties of regenerated cellulose.
1) viscosity, 2) copper number, 3) iodine number.

tervals where the phosphoric acid exists in the form of its hydrates: the monohydrate in the first case and the polyhydrate in the second, which emphasizes the essential role played by hydrates in the solution of cellulose in concentrated electrolyte solutions.

3. Both regions of unlimited swelling on the solubility curve show increase with reduction in the degree of polymerization of cellulosic material, in which connection this increase proceeds only toward lower acid concentrations. In this connection the absolute values of the solubility in the region of incomplete solution increase.

4. The use of preliminary swelling (in water or in more dilute phosphoric acid) makes it possible to assure complete solution of the cellulosic material over the expanse of the whole curve, including the intermediate region between the maxima.

5. With reduction in the size of the bath, the solubility of cellulose in phosphoric acid is retarded and made lower, which is associated with the exclusively rapid increase in the viscosity of the solutions in measure with increase in their cellulose content.

6. The heating of concentrated cellulose solutions in phosphoric acid or their prolonged standing is accompanied by noticeable impairment of the keeping properties of cellulosic material only if the heating is above 30–35° or the duration of standing more than a day. In its properties the hydrocellulose, obtained from a 4% solution of linters in 84% phosphoric acid that had been subjected to short heating (1 hour) at 40–50° or had been allowed to stand at room temperature for 4–6 days, lies close to the ordinary technical cellulose hydrates, for example, rayon.

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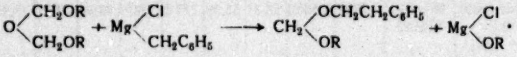
STUDY OF THE REACTION FOR THE EXCHANGE OF ALKOXYL GROUPS BY THE RADICALS OF ORGANOMAGNESIUM COMPOUNDS

A NEW METHOD FOR THE PREPARATION OF MIXED ACETALS OF FORMALDEHYDE WITH THE β-PHENYLETHYL ALCOHOL RESIDUE

M. R. Kulibekov and Shamkhal Mamedov

The acetals of formaldehyde with the β-phenylethyl radical in the molecule have been left completely unstudied due to the absence of suitable methods for their synthesis, and also because of their uneconomic preparation from β-phenylethyl alcohol. A. E. Chichibabin and S. A. Elgazin [1] were the first to demonstrate the possibility of replacing the ethoxyl group in acetals by the radical of organomagnesium compounds. When the primary ethers of dimethylene glycol are treated with organomagnesium compounds, one of the alkoxyl groups of the ether is replaced by the alkyl group of the Grignard reagent, forming the corresponding acetal of formaldehyde.

This caused us to run a series of experiments with benzylmagnesium chloride for the purpose of ob aining the mixed acetals of formaldehyde with β-phenylethyl alcohol, as a result of which we synthesized four new acetals of β-phenylethyl alcohol.



All of the synthesized acetals proved to be clear liquids with a delicate floral odor, in which connection the aromacity of the odor increases in measure with increase in the molecular weight. We are of the opinion that these acetals can find practical use in the perfumery industry, since they are not inferior to β-phenylethyl alcohol in aromacity. They are insoluble in water, but readily soluble in organic solvents.

EXPERIMENTAL

1. Preparation of the Ethyl β-Phenylethyl Acetal of Formaldehyde. To the organomagnesium compound, prepared in the usual manner from 2.4 g of magnesium and 12.65 g of freshly distilled benzyl chloride (b.p. 179°), was added in drops 13.4 g of the bis-diethyl ether of dimethylene glycol (b.p. 140–142°, d_4^{20} 0.9219, n_D^{20} 1.3595). Toward the end, the reaction flask was heated on the water bath for 2 hours with constant stirring. The next day the dark-green product was decomposed with water. The water layer was found to contain alcohol. The ether layer was washed with water and dilute soda solution, and then dried over anhydrous Na_2SO_4. Removal of the ether by distillation gave 9 g (50%) of product.

B.p. 98–101° (5 mm), n_D^{20} 1.5050, d_4^{20} 1.0021, MRD 53.27; Calc. 53.38.
Found %: C 72.88; H 9.17; M 179.1. $C_{11}H_{16}O_2$. Calculated %: C 73.33; H 8.88; M 180.

The ethyl β-phenylethyl acetal is a clear liquid with a delicate floral odor. It is insoluble in water, and readily soluble in alcohol, acetone and chloroform. An aqueous-alcohol solution of the acetal has a delicate odor. This acetal is new in the chemical literature.

Hydrolysis of the Ethyl β-Phenylethyl Acetal of Formaldehyde. To determine its structure the ethyl β-phenylethyl acetal of formaldehyde was subjected to hydrolysis in the presence of sulfuric acid.

To 60 ml of distilled water, acidified with 3 ml of concentrated sulfuric acid, in a small round-bottomed flask with mechanical stirrer and reflux condenser, was added 3.5 g of the ethyl β-phenylethyl acetal of formaldehyde. In view of the fact that the acetal corresponds to a primary alcohol, the hydrolysis of this acetal in comparison to the acetals of seconcary and tertiary alcohols [2] is very difficult, i.e., it requires drastic reaction conditions, for which reason the reaction flask was heated in a sand bath for 30–40 hours with mechanical stirring. We isolated 2.8 g of liquid with b.p. 92–95° (5 mm) from the hydrolysis. Study revealed that it is benzylcarbinol:

d_4^{20} 1.0209, n_D^{20} 1.5320, MR 37.02; Calc. MR 37.77 [3, 4].

The mother liquor was qualitatively shown to contain ethyl alcohol and formaldehyde. The fact that benzylcarbinol, and also ethyl alcohol and formaldehyde, were obtained in the hydrolysis of the ethyl β-phenylethyl acetal supports the validity of the structure assigned to the obtained acetal.

The method used to study the other acetals of formaldehyde prepared by us was similar to the preceding. Their physicochemical constants are presented in the table.

Physicochemical Properties of the Synthesized Acetals

$$CH_2\begin{matrix}OCH_2{-}CH_2{-}C_6H_5\\ OR\end{matrix}$$

Name of substance	Boiling point	d_4^{20}	n_D^{20}	MR found	MR calculated	M found	M calculated	Analysis data (%) found C	Analysis data (%) found H	Analysis data (%) calculated C	Analysis data (%) calculated H
Formaldehyde ethyl β-phenylethyl acetal (R = C_2H_5)	98–101° (5mm)	1.0021	1.5050	53.27	53.38	179.1	180	72.88	9.17	73.33	8.88
Formaldehyde butyl β-phenylethyl acetal (R = n-C_4H_9)	112–114 (7mm)	0.9660	1.4900	62.24	62.62	204.4	208	75.50	9.92	75.00	9.61
Formaldehyde isoamyl β-phenylethyl acetyl (R = iso-C_5H_{11})	118–121 (18mm)	0.9634	1.4930	66.84	66.54	221.1	222	75.17	9.96	75.67	9.91
Formaldehyde hexyl β-phenylethyl acetal (R = n-C_6H_{13})	118–120 (13mm)	0.9560	1.4952	72.01	71.16	234.7	236	75.73	10.32	76.27	10.17

SUMMARY

1. A new method was developed for the synthesis of the acetals of β-phenylethyl alcohol, involving the reaction of dimethylene glycol ethers with benzylmagnesium chloride. Four new acetals of formaldehyde were synthesized in yields of 47–50%.

2. All of the synthesized acetals proved to be liquids with a delicate floral odor; here it was established that they are not inferior to β-phenylethyl alcohol in odor, and that the aromacity of odor increases in measure with increase in molecular weight.

3. It was shown that under drastic conditions these acetals suffer hydrolysis, forming β-phenylethyl alcohol.

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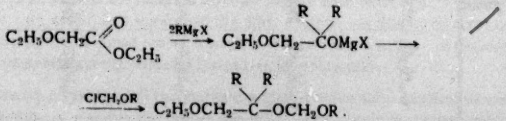
*T. p. = C. B. Translation pagination.

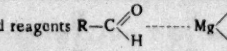
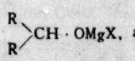
XXVII. SYNTHESIS OF THE β-ALKOXY DERIVATIVES OF METHYLENE GLYCOL ETHERS

Shamkhal Mamedov and G. Mamedov

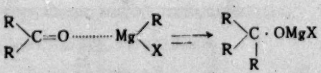
Earlier we had described the synthesis of some γ-alkoxy derivatives of the methylene glycol ethers [1]. The "organomagnesium" method of synthesizing ethers, proposed by one of us [2], was used in the synthesis. The purpose of the present study was to investigate the possibility of using the "organomagnesium" method in the synthesis of the β-alkoxy derivatives of the methylene glycol ethers. This class of polyglycol ethers has hardly been studied.

Our experiments on the matter revealed that the indicated ethers can be easily synthesized by the above indicated method, if the esters of alkoxycarboxylic acids are used in the reaction. The reaction for the synthesis of the β-alkoxy derivatives of the methylene glycol ethers can be depicted by the equation:

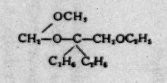
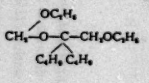
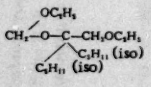
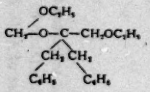


In explaining the mechanism of the action of organomagnesium halides on esters, Grignard [4] used the scheme of A. M. Zaitsev [3], assuming the formation of the magnesium haloalcoholates of tertiary and secondary alcohols. Some of the anomalous courses of this reaction, first revealed by Grignard [5] and other investigators [6], received their explanation in the studies of G. L. Stadnikov [7]. I. Iotsich [8] showed that for a normal reaction course in the direction of forming the magnesium haloalcoholates of tertiary and secondary alcohols, the conditions and order of running the reaction play an essential role. Nevertheless, a paper by Hess and co-workers [9] appeared in print, disputing the validity of Grignard's scheme. According to the data of these authors, the reaction products of organomagnesium halides with carbonyl compounds are complexes of oxo compounds with the Grignard reagents  , migrating into alcohols under the influence of water, and not magnesium haloalcoholates of the type  , as had been indicated by Grignard.

Meisenheimer [10], coming out against Hess, admits the validity of the viewpoint that complexes are formed in the first phase of the reaction between organomagnesium halides and carbonyl compounds, which, in his opinion, gradually migrate into alcoholates.



The net result of the indicated studies was that the explanations of the mechanism of these reactions began to depart from the position taken by Grignard [11]. The discussion raised by Hess and co-workers received its final answer in the studies of A. N. Nesmeyanov and co-workers [12], who demonstrated the experimental errors present in the studies of Hess and co-workers, and also in Meisenheimer's study. A. N. Nesmeyanov and co-workers showed by the method of crystalloptical and chemical identification that the precipitates obtained in the reactions of aldehydes and ketones with alkylmagnesium halides are magnesium haloalcoholates.

Structural formula	Name of compounds	Boiling point (mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Gross weight formula	Molecular weight found	Molecular weight calculated	% : C found	% : C calculate	% : H found	% : H calculated	Yield (%)
	Methyl α,α-diethyl-β-ethoxyethyl ether of methylene glycol	84—85 (10)	0.8980	1.4200	53.54	53.31	$C_{10}H_{12}O_3$	185.87	190.00	63.16	63.57	12.24	11.58	50
	Ethyl α,α-dibutyl-β-ethoxyethyl ether of methylene glycol	127—130 (8)	0.8850	1.4312	76.08	76.40	$C_{15}H_{32}O_3$	256.15	260.0	69.11	69.23	12.78	12.31	42
	Ethyl α,α-diisoamyl-β-ethoxyethyl ether of methylene glycol	134—137 (10)	0.8800	1.4328	85.02	85.63	$C_{17}H_{36}O_3$	284.6	288.0	70.68	70.83	12.80	12.50	27
	Ethyl α,α-dibenzyl-β-ethoxyethyl ether of methylene glycol	224—225 (8)	1.0520	1.5470	98.88	98.31	$C_{21}H_{28}O_3$	324.23	328.0	76.59	76.83	8.81	8.54	30

Our numerous syntheses [13] of methylene glycol ethers using the "organomagnesium" method of synthesizing ethers, and also the experimental material of the present paper, are in complete agreement with the Grignard-Nesmeyanov scheme. When the factors influencing the direction of the reaction for the action of organomagnesium compounds on carboxylic acid esters are taken into consideration it becomes possible to achieve a maximum yield of the magnesium haloalcoholates, being the intermediate products in the synthesis of alcohols, and in our case, in the synthesis of the alkoxy derivatives of the methylene glycol ethers.

Taking all of the above into consideration, we developed conditions for applying the "organomagnesium" method of synthesizing ethers to the synthesis of the β-alkoxy derivatives of the methylene glycol ethers. The α-chloroethers, the necessary raw material in our syntheses, were obtained by the passage of a stream of dry hydrogen chloride through a mixture of trioxymethylene and the alcohol with some cooling [14]. The other component of the reaction, ethyl ethoxyacetate, was prepared by the method of [15].

EXPERIMENTAL

Synthesis of Methyl-α, α-Diethyl-β-ethoxyethyl Ether of Methylene Glycol. The organomagnesium compound was prepared in the usual manner from 2.5 g of magnesium and 12.0 g of ethyl bromide. To the flask through a dropping funnel was slowly added 6.0 g of dry ethyl ethoxyacetate with cooling. The reaction mixture was allowed to stand for 3 hours at room temperature, after which with constant stirring and cooling was added 8.0 g of chloromethyl ether, and the reaction mixture was let stand overnight. The next day the flask contents were decomposed with acidulated water, and the ether solution was dried over fused calcium chloride. After distilling off the solvent, the obtained reaction product was vacuum-distilled. Redistillation gave 4.3 g of the methyl-α, α-diethyl-β-ethoxyethyl ether of methylene glycol (table).

Three other new β-alkoxy derivatives of the methylene glycol ethers were synthesized under similar conditions, the constants of which are given in the table. All of the synthesized alkoxy derivatives of the methylene glycol ethers are liquids with a pleasant odor, insoluble in water, and readily soluble in ether, benzene and the alcohols.

SUMMARY

1. The "organomagnesium" method of synthesizing ethers can be used to synthesize the alkoxy derivatives of the methylene glycol ethers.

2. Four new members of the β-alkoxy derivatives of the methylene glycol ethers were synthesized.

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THE SYNTHESIS OF NONSTEROID ANDROGENS

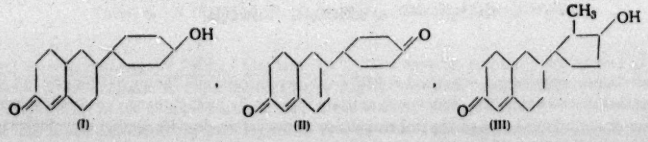
A. M. Khaletsky and B. A. Zaputryaev*

Whereas the replacement of naturally occurring steroid estrogens—estrone, estradione etc. has been very successfully achieved by the synthesis of derivatives of p,p'-dihydroxydiaryl-butane, hexane and octane, or of the corresponding unsaturated compounds (stilbestrol), or of arylhalogenoethylenes (triphenylbromoethylene, diphenylnaphthylbromoethylene etc.)[1], the synthesis of nonsteroid androgens is still practically an unsolved problem, in spite of different attempts by a number of authors working in this field [2].

From the similarity in structure of the natural estrogens and androgens, for example, estrone and testosterone [1], it has been suggested that a corresponding similarity may be sought in the nonsteroid substitutes. With this in mind Wilds and coworkers [3] synthesized various analogs of stilbestrol [1], having either a fully or a partly hydrogenated aromatic ring and differing also in the degree of oxidation of the corresponding cyclohexyl derivatives. Although the cyclohexanol and cyclohexanone derivatives obtained showed androgenic activity, they did so to such an insignificant extent that they could be of no practical importance. At the same time it was shown that, for example, 3-p-hydroxyphenyl-4-hydroxycyclohexylhexane still retains some estrogenic activity; 3-cyclohexanol-4-cyclohexanonchexane, on the other hand, does not.

In a study of the influence of different rings and groups in the androgen molecule the same workers synthesized a series of analogs of testosterone with no C ring and no angular methyl group. The authors drew particular attention to the first compounds they synthesized—6-(cyclohexanol-4')- and 6-(cyclohexanone-4')-$\Delta^{1(9)}$-octalone-2, structures (I and II), which showed androgenic activity in doses of 1.5-2.5 mg. Recently, however, these authors withdrew their reports on the biological activity of the materials described, pointing out that none of the compounds which they synthesized have androgenic activity [4].

In an attempt to imitate more closely the structure of natural androgens with no C ring, Z. A. Pyrakhina [5] synthesized 6-(2'-methylcyclopentanone-3)-$\Delta^{1(9)}$-octalone-2, structure (III), giving special importance to the methyl and carbonyl groups; this compound too, however, was inactive.



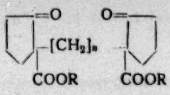
In this connection it is of interest to note the recently synthesized derivatives of perhydrochrysene [6, 7], which differ from the natural androgens by the presence of a D six-membered ring and by the absence of one or even two angular groups, yet which have androgenic activity (10% of that of testosterone). This shows that the presence of a five-membered ring and an angular methyl group is not necessary for androgenic activity.

Recent work by I. N. Nazarov and coworkers [8] shows fairly conclusively that when the A ring of 6-(2'-

* Abstract from B. A. Zaputryaev's Candidate's dissertation.

methylcyclopentanone-2)-$\Delta^{1(9)}$-octalone is made aromatic the compound does not acquire estrogenic properties, although it is closest to the estrone structure; thus further syntheses in the nonsteroid hormone series are required.

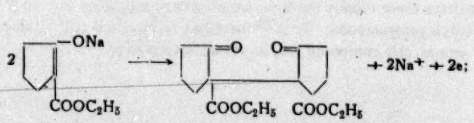
In connection with these points it seemed of interest to communicate some information concerning the synthesis of nonsteroid androgens carried out by us, especially as data recently published by Mayer and Alder [9] are closely concerned with the structures of the compounds synthesized by us. The authors synthesized the α, ω-polymethylenedicyclopentanonedicarboxylic esters of structure:



(in which n = 4 or 6 and R = CH_3 or C_2H_5) in order to check N. D. Zelinsky's reaction [10] between α,ω-dihalogeno hydrocarbon derivatives and the metal derivatives of cyclopentanonecarboxylic esters; as is known, in such cases the monohalogeno derivative is the chief product. The authors showed, however, that in the cases studied by them the α,ω-dihalogeno hydrocarbon derivatives react with 2 molecules of the cyclopentanonecarboxylic ester, forming the compounds given above.

The reaction studied by us between the potassium derivative of ethyl cyclopentanonecarboxylate and diiodomethane and also 1,2-dibromoethane have shown that whereas in the former case double condensation does not take place, in the latter case diethyl 1,2-dicyclopentanoneethanedicarboxylate is formed, with m.p. 104-106°, m.p. semicarbazone 223-224° (with decomposition), m.p. di-(2,4-dinitrophenylhydrazone) 247-248° (with decomposition).

In addition to the above compounds a study was made of the products of the electrolysis of the sodium derivative of ethyl cyclopentanonecarboxylate in aqueous methyl alcohol solution with current density 30 ma/cm^2, platinum anode, nickel cathode and 0.1 N caustic soda solution as catholyte. After electrolysis, distillation of the methyl alcohol, neutralization with hydrochloric acid and extraction with benzene, a material with m.p. 105-105.5° was isolated, which from analysis and by preparation of derivatives proved to be diethyl dicyclopentanone-2,2'-dicarboxylate-1,1'. Its formation may be represented by the reaction:



Its 2,4-dinitrophenylhdrazone melted at 264° (with decomposition). Biological tests on rats with the materials synthesized revealed that androgenic activity is shown by diethyl ethane- α,β-dicyclopentanone-2,2'-dicarboxylate at a minimum dose of 15γ; the magnitude of the active dose for diethyl dicyclopentanone-2,2'-dicarboxylate-1,1' has not yet been determined precisely.

We have to express our gratitude to B. P. Artamonov for directing the electrochemical work and to E. S. Rosova and E. V. Bugreeva for its execution, and also to T. A. Melnikova for the biological examination of the materials synthesized.

EXPERIMENTAL

The Potassium Derivative of Ethyl Cyclopentanone-2-Carboxylate-1. 84 g of 40 % caustic potash solution was added gradually with stirring below 2-3° to a solution of 93.8 g of ethyl cyclopentanone-2-carboxylate-1 in

93.8 ml of ethyl alcohol. After 3 hours the precipitated potassium derivative was filtered off, washed with alcohol and ether, and dried in a vacuum desiccator at 40–50°; yield 101.3 g (87.1%). Fine white crystalline powder with apparently one molecule of water of crystallization.

Found: equiv. 211.6. $C_8H_{11}O_5K \cdot H_2O$. Calculated: equiv. 212.3.

Diethyl α,β-dicyclopentanone-2,2'-ethanedicarboxylate. 479.1 g of the dry potassium derivative of ethyl cyclopentanone-2-carboxylate-1, 300 ml of dry toluene and 278 g of 1,2-dibromoethane were heated at 120–125°. Reaction was accompanied by the dissolution of the main bulk of the potassium derivative and the separation of potassium bromide, after which heating was continued for a further 92 hours. After the reaction the precipitate was filtered off, the filtrate treated with dilute hydrochloric acid and ice, the toluene layer removed, the aqueous layer extracted with toluene and the combined toluene solutions washed with water, 5% sodium carbonate solution, again with water, and dried over anhydrous sodium sulfate. After vacuum distillation of the toluene and dibromoethane the orange-red liquid residue was distilled; the following fractions were obtained: 30-80° at 13 mm–71.96 g; 70–123° at 2 mm–44.47 g; 106–153° at 1 mm–13.51 g; 135–201° at 1 mm–110.96 g and 76.11 g of tarry residue.

On standing for 12 hours the fraction with b.p. 135–201° at 1 mm yielded fine crystals which were filtered off and washed with alcohol; yield 3.25 g, m.p. 102–105°. After twice recrystallizing from 50% alcohol, m.p. 104–106°. Colorless plates, insoluble in water, sparingly soluble in alcohol, readily soluble on heating, soluble in ether.

Found %: C 64.18, 64.19; H 7.98, 7.95. M 325.8, 325.6. $C_{18}H_{22}O_6$. Calculated %: C 63.87; H 7.76. M 338.4.

The monosemicarbazone of diethyl α,β-dicyclopentanone-2,2'-ethanedicarboxylate, recrystallized from dilute acetic acid, melted at 223–224° (with decomposition).

Found %: N 10.50, 10.10. $C_{19}H_{29}O_6N_3$. Calculated %: N 10.62.

The di-(2,4-dinitrophenylhydrazone), recrystallized from a mixture of ethyl acetate and xylene (1:1), melted at 247–248° (with decomposition).

Found %: N 16.06, 16.02. $C_{30}H_{34}O_{12}N_8$. Calculated %: N 16.04.

Diethyl dicyclopentanone-2,2'-dicarboxylate-1,1'. The anolyte, prepared from 27.46 g of ethyl cyclopentanone-2-carboxylate, 4.05 g metallic sodium, 311 ml methanol and 37.8 ml water, was placed in the anode compartment of the electrolysis cell. The anode material was platinum, the cathode material nickel. The cathode and anode compartments were separated by a ceramic diaphragm. A 0.1 N caustic soda solution was used as catholyte. The anolyte was cooled by a coiled condenser to prevent loss of alcohol. Electrolysis was carried out at a current density of 30 ma/cm^2 for 1.5 hours; the process was judged at an end when the anolyte gave a neutral reaction. The anolytes from six experiments were combined and the methyl alcohol distilled in vacuo from the reaction liquid at 40°. The thick dark-colored liquid residue (180 g) was acidified with dilute hydrochloric acid (to congo red) and extracted five times with 100 ml portions of benzene. The benzene extracts were washed with sodium carbonate solution and water and dried over anhydrous sodium sulfate. After distilling off the benzene, 6 g of a light fraction was vacuum distilled at 65–100° and 25 mm. The residue of approximately 128 g of viscous orange-red opalescent liquid was fractionally distilled repeatedly in vacuo; a fraction distilling at 145–184° and 1 mm, and containing 10.3 g, partly crystallized. After separation of the crystals the filtrate was redistilled at 170–177° (1 mm); crystals again separated and were added to the first fraction. 1.6 g in all were

isolated and after recrystallization from 50% methyl alcohol melted at 105–105.5°. Fine white crystalline powder, insoluble in water, acid and alkali, readily soluble in alcohol, ether and benzene.

Found %: C 61.4, 61.9; H 7.17, 7.20. M 302.9. $C_{16}H_{22}O_6$. Calculated %: C 61.9; H 7.1. M 310.0.

The 2,4–dinitrophenylhydrazone after recrystallization from a mixture of alcohol and dichloroethane (1:1) formed yellow-orange crystals with m.p. 264° (with decomposition).

Found %: N 16.69, 16.74. $C_{28}H_{30}O_{12}N_8$. Calculated %: N 16.71.

SUMMARY

1. The reaction between the potassium derivative of ethyl cyclopentanonecarboxylate and dibromoethane in toluene has been studied, and diethyl α,β–dicyclopentanone–2,2'–ethanedicarboxylate–1,1' has been isolated.

2. The products of the electrolysis of the sodium derivative of ethyl cyclopentanone–2–carboxylate–1 (in methyl alcohol and water) have been studied; from these products diethyl dicyclopentanone–2,2'–dicarboxylate has been isolated.

3. Diethyl α,β–dicyclopentanone–2,2'–ethanedicarboxylate–1,1' has been tested biologically on rats; it has been found to show androgenic activity at a dose of 15 γ.

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THE SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

VI. THE OXIDATIVE CHLOROPHOSPHINATION OF CYCLOHEXANE AND PROPYLENE USING PHENYLDICHLOROPHOSPHINE

Yu. M. Zinovyev and L. Z. Soborovsky

The reactions between phosphorus trichloride and paraffinic, ethylenic and acetylenic hydrocarbons, their derivatives, and ethers have been carried out by us earlier [1-4]. It has also been shown that the formation of a phosphorus–carbon bond is also achieved when phosphorus trichloride is replaced by alkyldichlorophosphines [5].

In the present work the reactions between aryldichlorophosphines, hydrocarbons and oxygen have been studied. The aryldichlorophosphine used was phenyldichlorophosphine, the hydrocarbons–cyclohexane and propylene. Phenylcyclohexylphosphinyl chloride (I), phenylchloropropylphosphinyl chloride (II) and phenyldichlorophosphine oxide were isolated from the reaction mixture:

$$2C_6H_5PCl_2 + C_6H_{12} + O_2 \longrightarrow \underset{(I)}{C_6H_5(C_6H_{11})P(=O)Cl} + C_6H_5POCl_2 + HCl,$$

$$2C_6H_5PCl_2 + C_3H_6 + O_2 \longrightarrow \underset{(II)}{C_6H_5(C_3H_6Cl)P(=O)Cl} + C_6H_5POCl_2.$$

Phenylcyclohexylphosphinyl chloride is a viscous liquid, not decomposed by cold water. Hydrolysis takes place when the synthesized chloride is heated with dilute alkali. When the alkaline solution obtained is acidified, free phenylcyclohexylphosphinic acid separates as white crystals soluble in acetone.

Phenylchloropropylphosphinyl chloride is a colorless high-boiling liquid. Although this material distils like a pure compound within one degree it is possible that the product is a mixture of isomeric compounds differing in the position of the substituent in the alkyl radical [4]. Structural formulae are not, therefore, given for (II).

$$C_6H_5(CH_3CHClCH_2)P(=O)Cl \qquad C_6H_5(CH_3(CH_2Cl)CH)P(=O)Cl.$$

The reaction studied between hydrocarbons (or their derivatives), oxygen and phosphorus trichloride (or its partly substituted derivatives) is characterized by the following fundamental features: the formation of a new phosphorus–carbon bond and attachment of oxygen to the phosphorus atom, i.e. transfer of the latter from the trivalent state to the pentavalent; the organophosphorus compound thus formed always contains chlorine linked

to the phosphorus atom and when unsaturated hydrocarbons are used in the reaction, in the alkyl radical. It appears to us that all these features are expressed by referring to the reaction as the oxidative chloro-phosphination of the hydrocarbons concerned.

EXPERIMENTAL

1. Preparation of phenylcyclohexylphosphinyl chloride. Oxygen was passed at 10–15° through a mixture of 45 g phenyldichlorophosphine and 50 ml hexane until no more heat was evolved. After separation of unused hexane (22 ml) from the reaction mixture, the residue was fractionally distilled in vacuo. 30.7 g of phenyldichlorophosphine oxide with b. p. 120–130° (10 mm), was obtained, together with 11.1 g of a material which after two distillations boiled at 191–193° (6 mm), d_4^{20} 1.2096, n_D^{20} 1.5560. Yield 36%.

Found%: C 59.32, 59.50; H 5.68, 5.33; Cl 14.28; equiv. 1.99; MR_D 64.44. $C_{12}H_{16}OClP$. Calculated%: C 59.38; H 6.64; Cl 14.61; equiv. 2.00; MR_D 64.63.

2. Preparation of phenylcyclohexylphosphinic acid. 1.3 g of phenylcyclohexylphosphinyl chloride was warmed with 50 ml 0.5 N NaOH until the oil had completely dissolved. The cooled solution was acidified with hydrochloric acid using congo red indicator. The precipitated crystals were filtered off, washed with water until the washings were free from chloride ion and dried to constant weight. 1.0 g of material with m.p. 106° was obtained. Yield 83%.

Found %: C 63.74, 63.94; H 6.97, 6.74. $C_{12}H_{17}O_2P$. Calculated %: C 64.27; H 7.64.

3. Preparation of phenylchloropropylphosphinyl chloride. 25 g propylene was condensed into a solution of 45.0 g phenyldichlorophosphine in 50 ml chloroform cooled to −50°. Oxygen was passed through the mixture obtained for 70 hours. The temperature of the reaction liquid was kept at around -50°. The solvent was distilled from the reaction mixture and the residue fractionally distilled in vacuo. 3.4 g of material boiling at 140° (2 mm), d_4^{20} 1.2958, n_D^{20} 1.5510 was separated.

Found%: C 46.55, 46.44; H 5.03, 5.07; MR_D 58.21. $C_9H_{11}Cl_2OP$. Calculated %: C 45.59; H 4.67; MR_D 57.85.

SUMMARY

1. It has been shown that aryldichlorophosphines may be used instead of phosphorus trichloride or alkyldichlorophosphines as phosphinating agents in oxidative chlorophosphination of hydrocarbons (or their derivatives).

2. The mixed alkylarylphosphinyl chlorides—cyclohexylphenylphosphinyl chloride and chloropropylphenylphosphiny chloride have been prepared by the oxidative chlorophosphination of cyclohexane and of propylene using phenyldichlorophosphine.

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THE SYNTHESIS OF HALOGEN DERIVATIVES OF PHENAZINE

IV. BROMOPHENAZINES

V. P. Chernetsky and A. I. Kiprianov

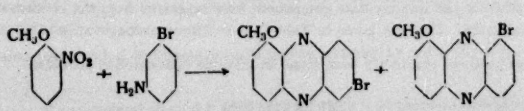
The bromoderivatives of phenazine have been little studied. 2-Bromophenazine has been prepared by the cyclization of 2-amino-4'-bromodiphenylamine [1]. The cyclization of halogenosubstituted o-nitrodiphenylamines has been proposed for the synthesis of 2-halogenophenazines [2], including 2-bromophenazine. The synthesis of 2,6-dibromophenazine [3] from p-bromonitrobenzene and also by alkaline condensation of p-bromonitrobenzene with p-bromoaniline according to Wohl and Aue has been described.

In a continuation of work on the synthesis of halogenophenazines [4-6] we obtained bromophenazines by a more accessible method—alkaline condensation of nitrobenzene and bromonitrobenzenes with aniline and bromoanilines in organic solvents. A pale yellow bromophenazine and a bright yellow N-oxybromophenazine were isolated from the products of the reaction between m-nitrobromobenzene and aniline. The bromophenazine had a melting point lower than that of the known 2-bromophenazine and gave a depression on taking mixed melting points; it was therefore 1-bromophenazine. The yellow N-oxide was reduced to 1-bromophenazine. As is known [5], the NO group in the N-oxyphenazines is formed from the nitro group. This N-oxide was therefore 10-oxy-1-bromophenazine. 9-Oxy-2-bromophenazine, which might also be expected to be formed, was not found in the alkali-insoluble reaction products. It was obtained in small amount by the condensation of nitrobenzene with p-bromoaniline. It was converted to 2-bromophenazine on reduction.

10-Oxy-2-bromophenazine, together with a small amount of 2-bromophenazine, was obtained by the reaction of p-nitrobromobenzene with aniline. A sample of the mixed 9- and 10-oxy-2-bromophenazines gave a large melting point depression. The formation of 9-oxy-2-bromophenazine by condensation of nitrobenzene with p-bromoaniline and of 10-oxy-2-bromophenazine by condensation of p-nitrobromobenzene with aniline is further confirmation that the NO group in the N-oxyphenazines is formed from the nitro group [5].

The aqueous alkaline solutions obtained during the treatment of the products of all these reactions were of a deep red color, indicating the presence of phenazinols—produced by replacement of the bromine atom by a hydroxy group [6].

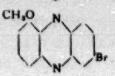
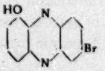
The condensation of o-nitroanisole with m-bromoaniline was also carried out. In this case it was expected that only 1-methoxy-6-bromo- and1-methoxy-8-bromophenazines could be obtained, and not their oxides, since the N-oxides with the peri-situated NO and OCH_3 groups should be unstable.



Both methoxybromophenazines were obtained. Their structure was proved by converting them to 1,6- and 1,8-dimethoxyphenazine and taking mixed melting points with the corresponding compounds prepared by alternative methods, when no depression was observed. The methoxybromophenazines were converted to the corresponding

hydroxybromophenazines by dealkylation with sulfuric acid and aluminum bromide. All the bromo derivatives of phenazine isolated by us are given with their melting points in Table 1.

TABLE 1

No.	Formula	Melting point
1		132–133°
2		148–149 [1]
3		188–189 (decomp. 206–208)
4		165–167 (decomp. 230)
5		163–164 (decomp. 210)
6		186–187
7		187–188
8		209–210
9		176–177

Several side-products and intermediate compounds were separated from the condensation products by chromatography on alumina. They are given in Table 2. 3,3'-Dibromoazoxybenzene (12) is of particular interest.

Azoxybenzenes have not previously been found in alkaline condensation products.

EXPERIMENTAL

The bromophenazines were obtained in the usual way [4-5]. The condensation products were separated and purified by chromatographing their benzene or toluene solutions on alumina and then crystallizing. In view of the fact that N-oxybromophenazines give salts which are sparingly soluble in acid solutions, they were separated by treating the benzene solutions of the appropriate chromatogram zones with 15 % hydrochloric acid. The orange

TABLE 2

No.	Formula	Melting point
10	m-$BrC_6H_4N=NC_6H_5$	69—70° [7]
11	p-$BrC_6H_4N=NC_6H_5$	94—95 [7]
12	m-$BrC_6H_4N=NC_6H_4Br$-m	107—109 [8]
	O	
13	o-$CH_3OC_6H_4N=NC_6H_4Br$-m	119—120
14	p-$BrC_6H_4NHC_6H_4NO_2$-o	167—168 [1]

salts were hydrolyzed by water, the bright yellow N-oxides dried and recrystallized from organic solvents.

The condensation of m-nitrobromobenzene with aniline. 20.2 g of m-nitrobromobenzene, 9.3 g aniline and 29.5 g powdered caustic potash were boiled in 150 ml of toluene for 4.5 hours. After chromatographing and crystallizing the following were obtained:

1-Bromophenazine. 1.8 g (6.9%), light yellow needles, from alcohol, m.p. 132-133°.

Found %: N 10.80, 10.79; Br 30.87, 31.01. $C_{12}H_7N_2Br$. Calculated %: N 10.81; Br 30.90.

10-Oxy-1-bromophenazine. 1.15 g (4.2%), bright yellow needles, from 50% alcohol, m.p. 188-189°, decomp. temp. 206-208°.

Found %: N 9.92, 9.96; Br 28.80, 28.93. $C_{12}H_7ON_2Br$. Calculated %: N 10.18; Br 29.10.

3-Bromoazobenzene. 3.1 g (11.9%), orange needles from alcohol, m. p. 69-70° [7].

Found %: N 10.79, 10.94; Br 30.50, 30.38. $C_{12}H_9N_2Br$. Calculated %: N 10.73; Br 30.65.

3,3'-Dibromoazoxybenzene. 5.79 g (16.2%), pale yellow leaflets from petroleum ether, m. p. 112-113°*.

Found %: N 8.10, 8.07; Br 44.90, 45.03. $C_{12}H_8ON_2Br_2$. Calculated %: N 7.87; Br 44.94.

A mixed melting point with 3,3'-dibromoazoxybenzene prepared by reduction of m-nitrobromobenzene gave no depression.

The condensation of p-nitrobromobenzene with aniline. 20.2 g p-nitrobromobenzene, 9.3 g aniline, 29.5 g powdered caustic potash and 150 ml benzene were boiled for 4 hours. The following were isolated:

2-Bromophenazine. 0.115 g (0.45%), light yellow needles from alcohol, m. p. 148-149° [1].

* M. p. According to [8] 109-110°.

Found %: N 10.73, 10.84; Br 30.86, 30.69. $C_{12}H_7N_2Br$. Calculated %: N 10.81; Br 30.90.

10-Oxy-2-bromophenazine. 2.82 g (10.2%), bright yellow needles from alcohol, m. p. 163-164°, decomp. temp. 210°.

Found %: N 10.19, 10.04; Br 28.85. $C_{12}H_7ON_2Br$. Calculated %: 10.18; Br 29.10.

The condensation of p-bromoaniline with nitrobenzene. 18.45 g nitrobenzene, 17.2 g p-bromoaniline and 29.5 g powdered caustic potash were condensed by boiling in 150 ml benzene for 3 hours. The following were isolated:

9-Oxy-2-bromophenazine. 1.7 g (6.2%), bright yellow needles from benzene, m. p. 165-167°, decomp. temp. 230°.

Found %: N 10.40, 10.41; Br 29.10, 28.92. $C_{12}H_7ON_2Br$. Calculated %: N 10.18; Br 29.10

A mixed melting point with the 9-oxy-2-bromophenazine and the 10-oxy-2-bromophenazine from the condensation of p-nitrobromobenzene with aniline melted at 145-155°.

4-Bromoazobenzene. 3.01 g (18.6%), orange needles from alcohol, m. p. 94-95°*

Found %: N 10.72, 10.85; Br 30.46, 30.52. $C_{12}H_9N_2Br$. Calculated %: N 10.73; Br 30.65.

4-Bromo-2'-nitrodiphenylamine. 2.2 g (7.5%), bright red needles from a large quantity of alcohol, m.p. 167-168° [1].

Found %: N 9.41, 9.51; Br 27.10. $C_{12}H_9O_2N_2Br$. Calculated %: N 9.55; Br 27.30.

A mixed melting point with 4-bromo-2'-nitrodiphenylamine prepared by a different method gave no depression.

The condensation of o-nitroanisole with m-bromoaniline. 45.9 g o-nitroanisole, 34.4 g m-bromoaniline and 60 g powdered caustic soda were boiled in 200 ml benzene for 10 hours. The following were isolated:

1-Methoxy-6-bromophenazine. 1.38 g (2.4%), yellow needles from benzene and ligroin, m. p. 186-187°.

Found %: N 9.68, 9.96; Br 27.69, 27.37. $C_{13}H_9ON_2Br$. Calculated %: 9.69; Br 27.68.

1-Methoxy-8-bromophenazine. 5.96 g (10.3%), yellow needles from benzene and ligroin, m. p. 187-188°.

* M. p. according to [7] 89°.

Found %: N 9.75, 9.82; Br 27.50, 27.60. $C_{13}H_9ON_2Br$. Calculated %: N 9.69; Br 27.68.

A mixture of this phenazine derivative with 1-methoxy-6-bromophenazine melted at 150-160°.

2-Methoxy-3'-bromoazobenzene. 1.4 g (2.4%), bright red needles from alcohol, m. p. 119-120°.

Found %: N 9.54, 9.80; Br 27.42, 27.73. $C_{13}H_{11}ON_2Br$. Calculated %: N 9.62; Br 27.49.

The dealkylation of methoxybromophenazines. 1-Hydroxy-6-bromophenazine. 0.25 g of 1-methoxy-6-bromophenazine was dissolved in 10 ml of benzene, 0.5 g of aluminum bromide added, and the brown mixture boiled under reflux for 6 hours. The dark brown complex obtained on cooling was broken down with a small quantity of finely-powdered ice. The orange-yellow mixture was made just alkaline and the blue-violet solution filtered through paper. The hydroxybromophenazine was precipitated from the solution with dilute acetic acid. Orange needles from ligroin. Weight 0.212 g (89%), m.p. 209-210°.

Found %: N 10.19, 10.29; Br 28.96, 29.20. $C_{12}H_7ON_2Br$. Calculated %: N 10.18; Br 29.01.

1-Hydroxy-8-bromophenazine. 1.1 g 1-methoxy-8-bromophenazine was heated with 60 ml of 60% sulfuric acid for 30 minutes. When dealkylation was complete (a drop of solution in dilute alkali gave a transparent crimson solution) the liquid was poured into 50 ml water, filtered, and caustic soda solution added until only faintly acid. The yellow hydroxy derivative which precipitated was filtered off and dried. Yield 1.07 g (quantitative). Bright yellow needles from alcohol, m. p. 176-177° in a sealed capillary.

Found %: N 10.00; Br 28.70. $C_{12}H_7ON_2Br$. Calculated %: 10.18; Br 29.01.

SUMMARY

1. 1- and 2-bromophenazines, 10-oxy-1-bromophenazine, 9- and 10-oxy-2-bromophenazines, 1-methoxy-6- and 8-bromophenazines have been prepared by alkaline condensation of nitrobenzene and bromonitrobenzenes with aniline and bromoanilines in organic solvents.

2. Various intermediate and side-products have been isolated from the alkaline condensation products: 3 and 4-bromoazobenzenes, 3,3'-dibromoazoxybenzene, 2-methoxy-3'-bromoazobenzene and 4-bromo-2'-nitrodiphenylamine.

3. 1-Hydroxy-6- and 8-bromophenazines have been prepared from the corresponding methoxybromophenazines by dealkylation.

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STUDIES IN THE FIELD OF AZOMETHINE DYES

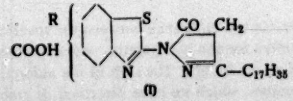
III. AZOMETHINE DYES FROM 3-ALKYL-1-(CARBOXY AND DICARBOXYBENZTHIAZOLYL-2')-PYRAZOLONES-5

I. A. Solovyeva, M. V. Krasheninnikova and G. I. Arbuzov*

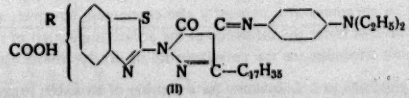
Azomethine dyes from pyrazolone-5 derivatives are widely used to obtain a purple image in multi-layer cinephotographic materials by the color development method. These dyes as a rule have two absorption bands in the visible spectrum, the maximum of the principal band lying usually at 510-550 mμ, that of the supplementary band at 410-440 mμ. The position of these bands and the ratio of their intensities, which determine the selectivity of absorption by the dye, depend to a considerable extent on the nature of the substituents in the 1- and 3-positions of the pyrazolone ring.

A. Weissberger and coworkers [1] and R. Gerbaux [2], studying the relationship between the structure of azomethine dyes of the pyrazolone series and their color, have shown that the introduction of the benzthiazole-2' residue into the 1-position of the pyrazolone ring noticeably lowers the intensity of the supplementary absorption band of the dyes, which consequently show a more selective absorption. Similar phenomena are reported in the patent literature [3].

In this connection it seemed of interest to study the compounds of this group in more detail. With this aim we synthesized 1-benzthiazolyl-(2')-3-heptadecylpyrazolone-5(5'-and 6'- mono- and 5',7'-,5',6'- and 6',7'-di)- carboxylic acids (I, R = H or COOH) and from them the azomethine dyes (II) (R= H or COOH).



(I)



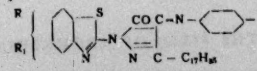
(II)

The pyrazolone derivatives shown above were obtained by condensation of ethyl stearoylacetate with 2-hydrazinobenzthiazolemono-or dicarboxylic acids in aqueous propanol solution on heating [see 4]. Most of the original hydrazines were synthesized by the reaction of the corresponding 2-amino-benzthiazole derivatives with hydrazine hydrate [5]. 2-Hydrazinobenzthiazole-5-carboxylic acid was obtained by oxidation of the 2-mercapto derivative [7] with sodium hypochlorite followed by treatment of the 2-sulfobenzthiazole-5-carboxylic acid formed with hydrazine hydrate at 0°.

* Deceased.

The synthesis of the azomethine dyes was achieved by heating the corresponding pyrazolone-5 derivatives with p-nitrosodiethylaniline in alcohol solution in the presence of piperidine. The absorption maxima of the synthesized dyes in alcohol solution and as obtained by color development in a gelatin layer, together with the ratio of the intensities of their principal and supplementary absorption bands in this layer (K) are given in Table 1.

TABLE 1



No	Substituent in the benzthiazole residue		Absorption maximum (in mμ)		K
	R	R_1	alcohol solution	gelatin layer	
1*	H	H	548	550	2.5
2	5—COOH	H	551	540	3.4
3	6—COOH	H	549	—	—
4	5—COOH	7—COOH	549	525	2.7
5	5—COOH	6—COOH	555	550	2.9
6	6—COOH	7—COOH	550	540	2.4
7**	1-(4'-carboxyphenyl)		—	525	2.0

*CH_3 group in the 3-position.

**A dye with an aryl group in the 1-position of the pyrazolone ring is given for comparison.

It can be seen from the data given that the introduction of carboxyl groups into the benzthiazole residue has very little influence on the position of the absorption maximum of the dyes in alcohol solution. Only in the case of the 5,6-dicarboxy derivative does a slight deepening of color take place. On changing from alcohol solutions to gelatin layers the absorption maximum of the dye from 1-(benzthiazolyl-2')-3-methylpyrazolone is practically unchanged. With the non-diffusing dyes with carboxyl groups a pronounced hypsochromic shift of the absorption maximum is observed, amounting to 5 mμ for the 5,6-derivative, 10-11 mμ for the 5-and 6,7-derivatives and reaching 24 mμ in the case of the 5,7-dicarboxy derivative. The selectivity of absorption in a gelatin layer of dyes with the benzthiazole residue proved in all cases to be greater than that of the dye with the carboxyphenyl group.

P. Vittum and A. Weissberger explain the difference between the spectral absorption of azomethine and indamine dyes in alcohol solution and when formed in a gelatin layer by color development as due to the difference in the degree of dispersion in these media [6]. The shift of the absorption maximum of the dyes on going from alcohol solutions to a gelatin medium, which we have described, is probably partly explained by the change in their state of aggregation. The phenomenon is evidently also connected, however, with a change in the electronic structure of the azomethines under the influence of the polarizing action of the medium, which may make itself felt to a varying extent depending on the polarizability of the dye molecule.

The authors express their gratitude to I. I. Levkoev for a number of valuable suggestions made in the course of this work.

EXPERIMENTAL

(with A. G. Guseva)

2-Mercaptobenzthiazole-5-carboxylic acid [7]. 4.1 g of 4-chloro-3-nitrobenzoic acid (0.02 mole) and 1.0 g of caustic soda were dissolved by heating in 25 ml water. A solution of sodium polysulfide, obtained by heating a mixture of 12.6 g of crystalline sodium sulfide (0.05 mole), 4.7 g sulfur (0.15 mole) and 13 ml water, was added to the solution and the reaction was stirred with heating on a water bath in a flask with reflux condenser for 2 hours. 3.05 g carbon disulfide (0.04 mole) was then added to the mixture, and heating continued for a further

TABLE 2

Name of compound	Quantity of hydrazine (g)	Quantity of stearoylacetate (g)	Temperature of bath	Time of heating (in hours)	Yield of product (%) crude	Yield of product (%) pure	Solvent used for crystallization	Appearance	Melting point	Analysis Found % : N	Analysis Formula	Analysis Calculated % : N
1-(5'-Carboxybenzthiazolyl-2')-3-heptadecylpyrazolone-5	2.09	3.9	110°	2.5	70	56	Ethyl alcohol	Light yellow crystals	~300°	8.54	$C_{28}H_{41}O_3N_3S$	8.42
1-(6'-Carboxybenzthiazolyl-2')-3-heptadecylpyrazolone-5	4.18	7.8	110	3	76.1	61.2	Glacial acetic acid	Faintly yellow crystals	~300	8.68	$C_{28}H_{41}O_3N_3S$	8.42
1-(5',7'-Dicarboxybenzthiazolyl-2')-3-heptadecylpyrazolone-5	2.53	3.9	100	4	67.5	40	Methyl alcohol	Colorless crystals	296-297	7.63	$C_{29}H_{41}O_5N_3S$	7.73
1-(5',6'-Dicarboxybenzthiazolyl-2')-3-heptadecylpyrazolone-5	2.53	3.9	100	3	63.0	34.6	Glacial acetic acid	Light yellow crystals	233-234	7.81	$C_{29}H_{41}O_5N_3S$	7.73
1-6',7'-Dicarboxybenzthiazolyl-2')-3-heptadecylpyrazolone-5	2.53	3.9	100	3	64.0	40.7	Glacial acetic acid	Light yellow crystals	204-205	7.88	$C_{29}H_{41}O_5N_3S$	7.73

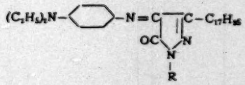


TABLE 3

R	Method of separating dye from reaction mass	Yield of dye (%) (crude)	Solvent used for crystallization	Appearance	Melting point	Analysis		
						Found	Calculated	
						%N	Formula	%N
5'-Carboxybenzthiazolyl-2'	Crystallized on cooling	38	Ethyl alcohol	Dark violet crystals	249–250°	10.55	$C_{38}H_{53}O_3N_5S$	10.62
6'-Carboxybenzthiazolyl-2'	25 ml saturated sodium chloride solution added	83.3	Glacial acetic acid	Brown crystals	182–183	10.62	$C_{38}H_{53}O_3N_5S$	10.62
5',7'-Dicarboxybenzthiazolyl-2'	100 ml ether added	84.3	Ditto	Dark violet plates	218–219	9.66	$C_{39}H_{53}O_5N_5S$	9.95
5',6'-Dicarboxybenzthiazolyl-2'	Ditto	72.5	"	Dark violet crystals	165–167	9.98	$C_{39}H_{53}O_5N_5S$	9.95
6',7'-Dicarboxybenzthiazolyl-2'	"	65.4	"	Violet crystals	185–186	10.01	$C_{39}H_{53}O_5N_5S$	9.95

15 hours (considerable evolution of hydrogen sulfide). The cooled reaction mass was acidified with acetic acid, the precipitate filtered off, washed with water and dissolved in water by addition of sodium carbonate. The precipitate of sulfur was filtered off, the solution acidified with acetic acid and the 2-mercaptobenzthiazole-5-carboxylic acid which separated was filtered off, washed with water and dried. Yield 3.84 g (91%). M. p. 298-301°. The product was purified by crystallization from ethyl alcohol. Colorless crystalline powder, sparingly soluble in ethyl alcohol, insoluble in benzene and ether. M.p. 300-303° (m.p. above 270° [7]).

Found %: N 6.85; equiv. 104.4. $C_7H_5O_4NS_2$. Calculated %: N 6.63; equiv. 105.5.

2-Hydrazinobenzthiazole-5-carboxylic acid. 2.1 g of 2-mercaptobenzthiazole-5-carboxylic acid (0.01 mole) was dissolved in a mixture of 3 ml 40% caustic soda solution and 3 g ice; 15.6 ml 18% sodium hypochlorite solution was then added slowly with stirring at 0-5°. The sodium salt of 2-sulfobenzthiazole-5-carboxylic acid which separated was filtered off, dissolved in 6 ml water, and a solution of 3 ml hydrazine hydrate in 4 ml water added with stirring below 0°. After 12 hours the reaction mass was made faintly acid to congo red with hydrochloric acid, the precipitate obtained filtered off, dissolved in 20 ml of 15% sodium acetate solution, the solution filtered and the product again separated with hydrochloric acid, filtered off, washed with water and dried at 70°. Yield 1.55 g (74%). Colorless crystals. Almost insoluble in the usual organic solvents, readily soluble in warm sodium acetate solution. M.p. above 300°.

Found %: N 19.80; equiv. 210.0. $C_8H_7O_2N_3S$. Calculated %: N 20.09; equiv. 209.1.

Pyrazolone-5 derivatives. 0.02 mole 2-hydrazinobenzthiazolemono- or dicarboxylic acid [3] was dissolved in 25 ml water with the addition of 5 ml 20% cuastic soda solution and the solution acidified with 5 ml of acetic acid. To the suspension of the freshly-precipitated hydrazine obtained a solution of 7.8 g of ethyl stearoylacetate (0.022 mole) in 40 ml propyl alcohol was added and the reaction mass heated in a flask with reflux condenser on a water or oil bath with stirring. After cooling, the mixture was diluted with 100 ml water, acidified to congo red with hydrochloric acid, the precipitate filtered off, washed with water and methyl alcohol and purified by crystallization. The experimental conditions, the properties of the pyrazolones obtained and the analysis data are given in Table 2.

Azomethine dyes. 0.001 mole of pyrazolone derivative was dissolved by heating in 15 ml absolute ethyl alcohol, 0.0011 mole p-nitrosodiethylaniline and 0.001 mole piperidine were added to the solution and the mixture warmed for 2 hours on a water bath in a flask with reflux condenser. After 12 hours the dye which separated was filtered off, washed with alcohol and ether and purified by repeated crystallization. The dye yields, their properties, and the analysis results are given in Table 3.

SUMMARY

1. The synthesis of 1-(5'- and 6'- carboxybenzthiazolyl-2')- and 1-(5',6'-, 5',7'- and 6',7'-dicarboxybenzthiazolyl-2')-3-heptadecylpyrazolones has been carried out and the corresponding azomethine dyes prepared by condensation with p-nitrosodiethylaniline.

2. It has been shown that the introduction of carboxyl groups into the benzthiazole residue of the above azomethine dyes brings about a slight bathochromic shift of the absorption maxima, amounting to as much as 8 mμ in the case of the 5,6-dicarboxy derivative.

3. It has been established that on going from alcohol solutions to gelatin layers the color of the above dyes is lightened, while the magnitude of the hypsochromic shift changes to an extent depending on the number and position of the carboxyl groups in the benzthiazole residue.

4. It has been shown that in all the cases studied dyes formed by color development in a gelatin layer from pyrazolones containing a benzthiazole residue in the 1-position show greater selectivity of absorption than the analogous 1-aryl derivatives.

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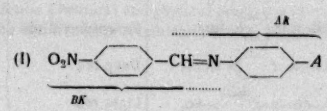
THE ANALYSIS OF THE INFLUENCE OF STRUCTURE ON SPECTRA

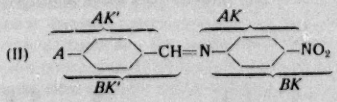
I. A COMPARATIVE STUDY OF COLOR IN AZOMETHINES OF TYPE $O_2NC_6H_4CH{=}NC_6H_4A$ AND $AC_6H_4CH{=}NC_6H_4NO_2$. REFLECTION AND ABSORPTION SPECTRA

V. A. Izmailsky and E. A. Smirnov

1. In a previous communication [1] we examined the azomethines with structures of type (I), where A is one of the electron-donating groups $-OH$, OCH_3, CH_3.



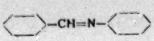
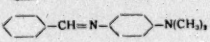
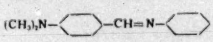
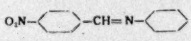
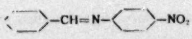
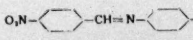
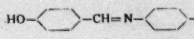
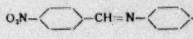
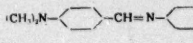
It was then established that replacement of the chromophoric azomethine group $-CH{=}N-$ by the $-CH_2NH-$ group not only does not lead to disappearance or even to a lightening of the color,* but, on the contrary, deepens it: the nitrobenzyl derivatives so prepared in the solid state usually have a somewhat deeper color than the corresponding azomethines. It was thus proved that the $-CH{=}N-$ chromophoric group present in the azomethines cannot be regarded as the fundamental chromophore responsible for the color of these compounds. The most essential requirement for color in azomethines is the presence of the electrophilic NO_2 group and the electron-donating [OH, OCH_3, N $(CH_3)_2$] groups, which, with the double bonds of the benzene nucleus, form the necessary complex system: the electrophilic BK and the electron-donating AK. The $-CH{=}N-$ group, being directly connected with each of these systems, exerts only a modifying action on them; at the same time, having a double bond, it may serve to transmit effects between these systems. The $-CH{=}N-$ group is, however, structurally unsymmetrical, so that the influence on color of the donor and electrophilic groups in a particular case should depend also on the position of these groups relative to the $-CH{=}N-$. Thus a comparative study of azomethines with structures of type (I) and azomethines with structures of type (II) is required.



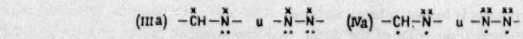
* Color is also observed in stilbene derivatives of analogous structure on replacing the $-CH{=}CH-$ group by the $-CH_2CH_2-$ group. Thus 4-nitro-4'-dimethylaminodibenzyl was obtained from alcohol and pyridine in the form of reddish-brown crystals with m.p. 220-221° [19].

In the present communication, compounds of these two types, containing OH or $N(CH_3)_2$ as the electron-donating groups (A), are examined. Compounds containing only one of the substituent groups: NO_2 or $N(CH_3)_2$, in a different position relative to the $-CH=N-$ group, are included for comparison (Table 1)•.

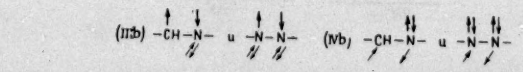
TABLE 1

Sp. no.	Formula of compound	Color of material	
		crystalline	powdered
1		Pale yellow	Almost colorless
2		Intense yellow	Bright yellow
3		Greenish yellow	Pale greenish-yellow
4		Yellow	Light yellow
5		Greenish yellow	Pale greenish-yellow
6		Yellow-brown	Orange-red
7		Brownish-yellow	Orange-yellow
8		Deep red	Cherry-red
9		Light red	Brown-orange

Study of the azomethines is particularly interesting in this respect, that for groups such as $-CH=N-$ and $-N=N-$, two types of conjugation may be predicted theoretically: 1) using the π-electrons of the double bond and 2) using the paired doublet from the N-atoms. If the electrons involved in conjugation are represented by the symbol (X), then the above groups, when they take part in the formation of a complex chromophoric system with delocalization of the π-electrons, may be represented by the following π-structural formulae (IIIa) and (IVa) [2,3].•• Electrons (single or from paired doublets) which are not involved in the delocalized conjugated π-system are represented as usual by points.



The electron-spin formulae (IIIb and IVb) with structures based on the principle of alternating spins are even more illuminating.•••



• In future each compound will be referred to by means of its appropriate number in Table 1.

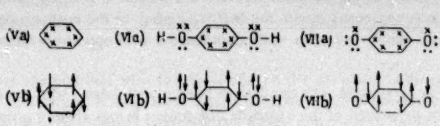
•• See following page.

••• See following page.

The π-electrons and the antiparallel nature of their spins are represented by arrows (↑ and ↓). The arrows lying vertically represent π-electrons taking part in the conjugation whose function axes are directed perpendicularly to the plane of the molecule. The arrows lying at a slant represent electrons whose function axes lie in the plane of the molecule and which are not involved in the delocalized π-structure of the molecule. Every two electrons with opposite spin are linked to one another.

The C-atom taking part in the double bond system of the $-CH=N-$ group conjugated with the benzene nucleus and containing π-electrons may be regarded as a C-atom in the "second valency state": all three σ-bonds lie in one plane while the Indian-club-shaped π-electron clouds lie perpendicularly to this plane [3b]. For the N-atoms of azomethine and azo-groups conjugated with a neighboring benzene nucleus by using the π-electrons of the double bond, we must allow an analogous structure for the N-atom in the "second valency state". In contrast to the second valency state of the C-atom, with three σ-bonds, in this case the N-atom has only two σ-bonds; the role of the electron pair of the third σ-bond is taken by the free paired doublet [see further (XXVII) and (XXIX)]. In (IVb) it is shown by the slanting position of the π-electron arrows that when one of the paired doublets of the N-atoms (indicated by the vertical arrows on the N-atoms) is conjugated with a neighboring benzene nucleus the function axes of the π-electrons of the double bond must lie in another plane perpendicular to the plane of the nucleus and are not therefore conjugated with this benzene nucleus [see further (XXVIII) and (XXX)].

By using π-structural and electron-spin formulae, in addition to giving a schematic picture of the composition and distribution of the π-electrons involved in the formation of the general conjugated π-electron system, we can reveal the reasons for the particular chemical and physical properties of a given π-electron system. As examples, π-structural (Va, VIa, VIIa) and electron-spin formulae (Vb, VIb, VIIb) are given for benzene, hydroquinone and p-benzoquinone [3].



Similar formulae also illustrate particularly well the phenomenon of increased electron-donating power in a system of two donating groups in the para-position, with the two donating groups in even positions relative to one another, for example, the two OH-groups in hydroquinone (VI), and the corresponding increased electrophilic nature of electrophilic groups; for example, the two CO-groups in p-benzoquinone (VII). The characteristic

** We obtain the π-structural formulae, which give the π-electron structure of the molecule, by breaking up all the π-bonds in the structural formula and adding the unshared paired electrons from N, S and O atoms taking part in the delocalized π-system. The paired doublets of the N-, O-, S-atoms are represented by the same symbols as the π-electrons in accordance with E. Huckel's suggestion [3a].

All the separate atomic components of the delocalized π-electronic system of the molecule are shown in the π-structural formula. π-Structural formulae and electron-spin formulae, which are a further development of the former, are special types of electronic formulae. We consider them superior to the old electronic formulae of molecules with conjugated systems (valency formulae with unshared electrons added) in that, besides other advantages, they do not require the often arbitrary choice of double bond position.

*** In the ground state of a conjugated system the spins of two neighboring π-electrons are opposed, and in all movements of π-electrons throughout the system the alternating sequence of the spins is preserved [3].

properties of (VI) and (VII) result from the presence of opposed polarizing influences (contrapolarized systems) together with the particular structure of the O-atoms and the particular structure of the benzene nuclei under their influence. The increased donating power of systems containing two donor N-atoms in the p-position is similarly explained (see further Section 5).

Thus the question has arisen as to whether it can be proved that the $-CH=N-$ group takes part in conjugation in two ways: not only in the ordinary way (IIIa or IIIb) but also in another special way (IVa or IVb) in the case where powerful electrophilic groups (NO_2) are present on the same side as the N-atom with electron-donating properties.

2. Visual observations and reflection spectra. The formulae of the compounds studied by us are given in Table 1 together with an indication of the color of the material in crystalline form and as a fine powder. It is of interest first of all to explain the influence on the color of the azomethine of the introduction of a particular single group—either the electrophilic NO_2 or the electron-donating $A = N(CH_3)_2$. From a comparison of the color of compounds 2 and 3 (Table 1) it can be seen that the introduction of the electron-donating $N(CH_3)_2$ group into the aniline component shows a much greater bathochromic effect than the introduction of the same group into the aldehyde component; compound 2 is bright yellow (in powder form) while compound 3 has only a pale greenish-yellow color. The presence of the electrophilic NO_2 group, on the contrary, has a greater effect when the group is found in the benzylidene component (see compounds 4 and 5, Table 1): compound 4 is light yellow in powder form, while compound 5 is only a pale greenish-yellow. From this it should naturally be expected that on the simultaneous introduction of both groups a more deeply colored compound would be obtained in the case where the donor group is introduced into the aniline component and the nitro group into the benzylidene component, i.e. that azomethines with structures of type (I) would be more deeply colored than azomethines of type (II). A comparison of compound 6 with 7, and 8 with 9, confirms the accuracy of this proposition; thus compound 6, in which the OH group lies in the aniline component and the NO_2 in the benzylidene component, has a red-orange color (in powder form) while the isomeric compound 7, with the groups situated in the reverse positions, is only pale yellow; compound 8 with the $N(CH_3)_2$-group in the aniline component and NO_2 in the benzylidene component has a cherry-red color while compound 9 with oppositely situated groups is only brown-orange.

Our observations are in agreement with the data of Mohlau and Adam, who established, for example, that an NO_2 group situated in the p-position of the aldehyde component brings about a greater deepening of color than the dimethylamino group in the same position; and that the latter, when situated in the aniline component, shows a bathochromic influence, etc. [4].

The visual observations are confirmed by the reflection spectra. Examination of the reflection spectra (Figures 1 and 2) shows that in all cases the reflection curves of azomethines with structures of type (I) are displaced relative to the curves of azomethines of type (II) towards the long-wave region (bathochromic), and that the shift is much greater for compounds containing both groups together (electrophilic and electron-donating) than for compounds containing only one of these groups.

3. Absorption spectra. As we have shown in an earlier communication, the absorption curves of azomethines with structures of type (I) are characterized by the presence first of all of a broad absorption band (a) with a well-defined maximum whose position depends on the relative strength of the electron-donating group: with increasing electron-donating power of a substituent this maximum is shifted regularly towards the long-wave region (Figure 3). The a-maximum is present not only in those compounds containing both electrophilic and electron-donating substituent groups simultaneously, but also in compounds with one of these groups, while the presence of the $N(CH_3)_2$ groups gives a more bathochromic position of the a-maximum than the presence of the NO_2 group (curves 2, 4). In the simplest of the azomethines—benzylideneaniline—the a-band is shown only as a sloping step. Azomethines of type (I) have, as well as an a-band, a second band with a maximum in the region 260-320 mμ (β-band). This band is very clearly defined in compounds containing substituent groups of both types A and B, and is considerably closer to the a-band in compounds containing only one of these groups.

In general the curves for azomethines of type (I) are typical curves for compounds with conjugated systems made up of two benzene nuclei joined by a group with a double bond ($-CH=CH-CH=N-$, $-N=N-$), and containing groups of opposite polarity on the ends (see further Sect. 4 and Figure 4).

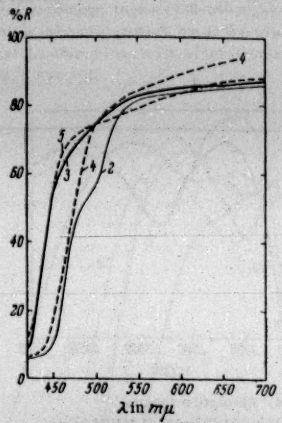


Fig. 1. Reflection spectra.
2) $C_6H_5CH{=}NC_6H_4N(CH_3)_2$-p;
3) p-$(CH_3)_2NC_6H_4CH{=}NC_6H_5$;
4) p-$O_2NC_6H_4CH{=}NC_6H_5$;
5) $C_6H_5CH{=}NC_6H_4NO_2$-p.

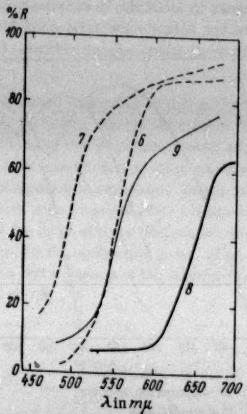


Fig. 2. Reflection spectra.
6) p-$O_2NC_6H_4CH{=}NC_6H_4OH$-p;
7) p-$HOC_6H_4CH{=}NC_6H_4NO_2$-p;
8) p-$O_2NC_6H_4CH{=}NC_6H_4N(CH_3)_2$-p;
9) p-$(CH_3)_2NC_6H_4CH{=}NC_6H_4NO_2$-p.

Absorption curves for azomethines with structures of type (II) are given in Figure 5. These curves are also characterized by the presence of a long-wave band with a well-defined maximum. This band is as a rule less broad than the α-band of azomethines of type (I) and differs moreover in having a greater intensity of absorption. The position of its maximum likewise depends on the character and relative strength of the substituent, but to a greater extent than with azomethines of type (I). Thus, for example, on going from benzylidene-p-nitroaniline (compound 5) to the corresponding p-hydroxy derivative (compound 7) the maximum is shifted by only + 12 mμ (Figure 5, Curves 5 and 7) whereas in the analogous change with azomethines of type (I) (compounds 4 and 5) the bathochromic shift of the maximum reaches + 41 mμ, i.e. it is approximately 2.5 times greater (Figure 5, Curves 4 and 6). On going from the p-p'-nitrohydroxy derivative (compound 7) to the p-p'-nitrodimethylamino derivative (compound 9) with azomethines of type (II) a bathochromic shift of the maximum of + 57 mμ results (Figure 5, Curves 7 and 9), while with azomethines of type (I) the shift is 72 mμ. It is interesting to note that the α-maximum of the curve of a compound containing only the $N(CH_3)_2$ group (without NO_2) has a somewhat more bathochromic position than the maximum of the curve of a compound containing OH- and NO_2-groups simultaneously (Figure 5, Curves 3 and 7), i.e. the introduction into the aldehyde component of benzylideneaniline of one N $(CH_3)_2$ group brings about a greater bathochromic effect than the simultaneous introduction of the OH- and NO_2-groups.

If the position of the α-maxima of the absorption curves of azomethines of type (I) is compared with the position of the α-maxima of the corresponding compounds of type (II) (Table 2), then in all cases the former have undergone a hypsochromic shift relative to the latter. The greatest magnitude (47 mμ) of this shift is reached with the compounds containing the NO_2- and N $(CH_3)_2$-groups simultaneously (compounds 8 and 9), the least, (3 mμ), with the compounds containing only the nitro group (compounds 4 and 5).

Since a shift of the absorption boundary (Table 2) takes place at the same time as the shift of the maxima, all the curves of azomethines of type (II) are found to have undergone a hypsochromic shift relative to the curves of azomethines of type (I). As a result, the former (Figure 5) are situated more closely together than the latter (Figure 3); the maximum bathochromic shift of the absorption boundary (at $\log\epsilon = 2$), observed on going from

benzylideneaniline (compound 1) to the p-p'-nitrodimethylamino derivative (compound 9), has a magnitude of 153 mμ, whereas in the corresponding change with azomethines of type (I) (compounds 1 and 8) it has a magnitude of 229 mμ.

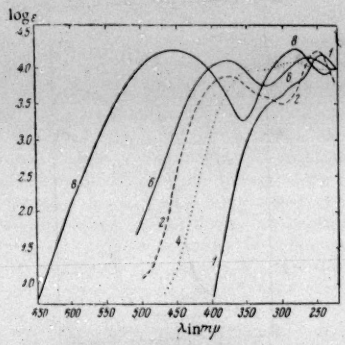


Fig. 3. Absorption spectra.
1) $C_6H_5CH=NC_6H_5$;
2) $C_6H_5CH=NC_6H_4N(CH_3)_2$-p;
4) p-$O_2NC_6H_4CH=NC_6H_5$;
6) p-$O_2NC_6H_4CH=NC_6H_4OH$-p;
8) p-$O_2NC_6H_4CH=NC_6H_4N(CH_3)_2$-p.

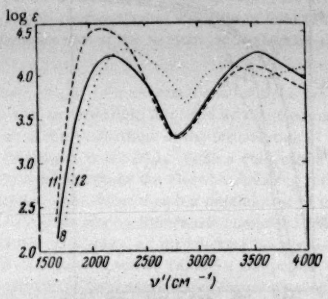


Fig. 4. Absorption spectra.
8) p-$O_2NC_6H_4CH=NC_6H_4N(CH_3)_2$-p;
11) p-$O_2NC_6H_4N=NC_6H_4N(CH_3)_2$-p;
12) p-$O_2NC_6H_4CH=CHC_6H_4N(CH_3)_2$-p.

TABLE 2

Sp. no.	Formula of compound	Position of maxima (in mμ) α	β	γ	Shift of λmax (in mμ)	Absorption boundary at log ε = 2	Shift of absorption boundary at log ε = 2*
1	$C_6H_5CH=NC_6H_5$	(300)*	(265)	244	—	375	—
2	$C_6H_5CH=NC_6H_4N(CH_3)_2$-p	376	(320)	250	0	461	0
3	p-$(CH_3)_2NC_6H=NC_6H_5$	356	—	238—240	—20	428	—33
4	p-$O_2NC_6H_4CH=NC_6H_5$	339	290	240	0	430	0
5	$C_6H_5CH=NC_6H_4NO_2$-p	336	—	—	—3	411	—19
6	p-$O_2NC_6H_4CH=NC_6H_4OH$-p	380	262,5	—	0	483	0
7	p-$HOC_6H_4CH=NC_6H_4NO_2$-p	348	—	—	—5	426	—57
8	p-$O_2NC_6H_4CH=NC_6H_4N(CH_3)_2$-p	452	282	—	0	604	0
9	p-$(CH_3)_2NC_6H_4CH=NC_6H_4NO_2$-p	405	(312)	—	—47	528	—76

In azomethines of type (II), with the exception of compound 9, there is no second clearly-defined maximum corresponding to the β-maximum of azomethines of type (I) lying in the region 260-320mμ. With the

*The position of the poorly-defined maxima (steps) given in brackets are only approximate. The shifts in λ in compounds 2 and 3, 4 and 5, 6 and 7, 8 and 9 are compared.

dimethylamino derivative (compound 3), as with benzylideneaniline, there is a clearly-defined maximum (γ) in the shorter wavelength region (238-240 mμ); with the other representatives of this series of compounds the same maximum is evidently present, but it is moved still further towards the short-wave region and was not measured. In general the absorption curves of the azomethines of type (II) resemble the absorption curve of p-nitroaniline (Figure 5, Curve 10).

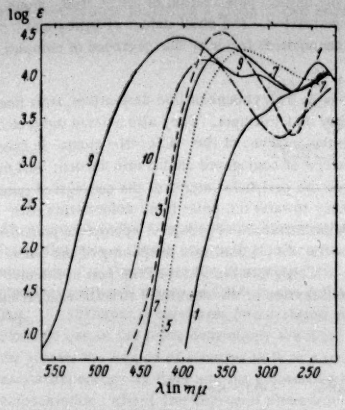


Fig. 5. Absorption spectra.
1) $C_6H_5CH=NC_6H_5$; 5) $C_6H_5CH=NC_6H_4NO_2$-p;
3) p-$(CH_3)_2NC_6H_4CH=NC_6H_5$;
7) p-$HOC_6H_4CH=NC_6H_4NO_2$-p;
9) p-$(CH_3)_2NC_6H_4CH=NC_6H_4NO_2$-p;
10) p-$H_2NC_6H_4NO_2$.

4. Possible approaches to the analysis of the influence of structure on color. Since azomethines have a structure closely related to that of azocompounds and stilbene derivatives, it is of interest first of all to examine how the color of these compounds is explained. Diltey and Vitsinger [5], starting from their theory of ionic chromophoric centers, explained the color of these compounds as arising from the acquisition, by the connecting group, of an inner ionic structure under the influence of the substituents in the benzene nuclei (A and B).

(VIII) A—⟨⟩—CH=CH—⟨⟩—B ⟶
⟶ A—⟨⟩—$\overset{+}{C}$H—$\overset{-}{C}$H—⟨⟩—B.

(IX) A—⟨⟩—N=N—⟨⟩—B ⟶
⟶ A—⟨⟩—$\overset{+}{N}$—$\overset{-}{N}$—⟨⟩—B.

The presence of "positivizing" (A) and negativizing (B) auxochromes" (electron-donating and electrophilic chromophores in our terminology [2]), especially when both are present together, is responsible for this polarization, as a result of which ionic chromophores which are coordinately unsaturated are formed (represented by asterisk in the formulae). Thus they point out that p-nitro-p'-dimethylaminostilbene (X) and p-nitro-p'-dimethylaminoazobenzene (XI) have a deep red color, while the corresponding compounds containing only the nitro group are of a pale yellow (XII) and red-orange (XIII) color, and, of the compounds which have no auxochromic group, (XIV) is colorless, (XV) is "yellow-orange" or "yellow-red" ([5], pp. 16 and 39).

(X) O_2N—⟨⟩—CH=CH—⟨⟩—$N(CH_3)_2$,

(XI) O_2N—⟨⟩—N=N—⟨⟩—$N(CH_3)_2$,

(XII) O_2N—⟨⟩—CH=CH—⟨⟩

(XIII) O_2N—⟨⟩—N=N—⟨⟩

(XIV) ⟨⟩—CH=CH—⟨⟩,

(XV) ⟨⟩—N=N—⟨⟩.

Diltey and Vitsinger regard azomethines as belonging to the class of compounds with inner-ionic chromophores, similar to stilbene derivatives and azo-compounds. They lose sight of the fact, however, that the –CH = N– group is unsymmetrical and even by itself has a certain degree of polarity: $-\overset{\delta+}{C}H=\overset{\delta-}{N}-$.

These authors pass over the problem of explaining, from their standpoint, the bathochromic action of electron-donating groups ("positivizing auxochromes") when these groups are situated in the aniline part of the azomethine molecule, i.e. in the case when they should weaken the natural polarization of the –CH=N– group. The improbable polarization $-CH-\overset{+}{N}=C-$ would then have to be postulated. The chief defect of Diltey and Vitsinger's theory lies in the fact that it does not consider the conjugation factor or the presence of complex delocalized chromophoric systems.*

Smets and Delvaux [6], in explaining the production of color in benzylideneaniline derivatives, start from theories which are to a certain extent related to the ideas of Diltey and Vitsinger. They also related the presence of color to the degree of internal-ionic polarization arising from the presence of the –CH=N– group. In contrast to Diltey and Vitsinger, however, these authors take the presence of conjugated chains into account, and, from the hypothesis of mesomeric shift, suggest that the charges arise on the peripheral atoms of the conjugated system. Taking account of the presence in the –CH=N–group of a tendency towards the polar ionic deformation $-\overset{+}{C}H-\overset{-}{N}-$, the authors consider that if this polarization is reinforced by the influence of groups in approprate positions, then as a result the mesomeric ionic shifts will be intensified and this should lead to a deepening of the color. Thus, for example, the introduction of the powerful donor group $N(CH_3)_2$ into the benzylidene part of the molecule should increase this tendency and bring about a shift in the direction of the quinonoid structures (XVI) and even (XVII):

(XVI) $(CH_3)_2\overset{+}{N}=C_6H_4=CH-\overset{-}{N}-C_6H_5$, (XVII) $(CH_3)_2\overset{+}{N}=C_6H_4=CH-N=C_6H_5^{-}$,

as a result of which, in the authors' opinion, the bathochromic shift of the maximum also arises. The same action is shown by other donor groups (OCH_3, OH) introduced into the benzylidene part of the molecule, but only to a much smaller extent corresponding to their weaker donor properties. The above authors could not, however, from the standpoint of the hypotheses which they developed, give a satisfactory explanation of the fact that the introduction of donor groups (for example OCH_3) into the aniline component also brings about a bathochromic effect which is even more pronounced than when the same group is introduced into the benzylidene component. "In the compound $C_6H_5CH=NC_6H_4OCH_3$ we observed exclusively bathochromic effect",–the authors write. "This effect is inexplicable and questionable, since the specimen evidently could not have been obtained in a normally pure state" ([6], p. 113). Our studies, however, confirm the observations of Smets and Delvaux and show that the bathochromic effect observed on the introduction of the donor OCH_3-group into the aniline part of the molecule (in the para-position) is not accidental, since the introduction into this position of the donor group $N(CH_3)_2$ also brings about a bathochromic shift of the maximum which is even greater than on introduction into the benzylidene part of the molecule.

A satisfactory explanation cannot be given from the opinion of Smets and Delvaux for the fact that the introduction of the nitro group into the para-position of the benzylidene part of the molecule brings about a powerful bathochromic effect. (The above authors confine themselves to an examination of the m-nitro derivatives).

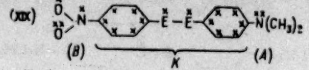
Thus the observed phenomena cannot be explained either from the Diltey-Vitsinger theory of ionic chromophoric centers or from the Smets and Delvaux theory connecting mesomeric shift and ionic polarization with the polar structure of the azomethine group. In general it must be admitted that attempts to seek an explanation for the color of such complex compounds as (X), No. 8, (XI) in the presence of the particular single chromophores

* Hertel [7] makes the same error when he considers the vinyl group –CH=CH– as the principal chromophore determining the color of stilbene derivatives and even of 4'-nitro-4-dimethylaminostilbene.

$-CH=CH-$, $-CH=N-$, $-N=N-$,* or in changes in the structure of these groups under the influence of polar substituents, are incorrect.

The spectra of all three of the above compound must be regarded as resulting from the presence of complex chromophoric systems of type B–K–A with similar π-electron structures. In all three compounds there is an identical conjugated system of 20 π-electrons** (XIX), where B–NO_2, A–N $(CH_3)_2$ and K– a conjugated system of 14 π-electrons including a group of two benzene nuclei with a double bond joining them into a single stystem.

(XIX)



(B) K (A)

$-\overset{N}{E}-\overset{N}{E}- = -\overset{N}{C}H-\overset{N}{C}H-, -\overset{N}{C}H-\overset{N}{N}-, -\overset{N}{N}-\overset{N}{N}-$

An approach to the analysis of the "chromo-state" [8,9] in conjugated compounds was shown at one time by Izmailsky from a theory connecting color with the degree of shift of electrons and bonds in the structure of the molecule: "... the weaker the absorption" [9].*** This conclusion was formulated in terms of the "meso-state" ("meso-structure") theory in 1918, in the following words: "The ideal**** desmotropic forms should be color-*****less. Different meso-forms (meso-states) correspond to colored forms, and those forms (states) which approach closer to one or the other desmotropy are more weakly colored" [10]. In other words, using modern terminology, the greater the degree of electron shift as a result of the conjugation of the interacting groups, the lower the excitation energy by light and the greater the bathochromic effect (the principle of the connection between bathochromic effect and degree of electronic shift). Thus there is a definite connection between the electron shift in the ground state and the tendency to undergo shift on changing from the ground state to an excited state of the molecule.

Similar conclusions were later reached by other authors. Thus the principle formulated by Lewis and Calvin in their well-known article [11] agrees in substance with the above ideas: "Every shift from the ideal state of a molecule makes further shift easier", "... the electron mobility is increased with increasing departure of the actual state of the molecule from the ideal state given by the classical structure".

Applying this theory to the three compounds indicated (X), (XI), No. 8, and in general to azomethines of type (I), we must regard their color and spectrum as resulting from delocalization into a single structure and the

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* It is of course true that these groups must be considered as the fundamental chromophores in such simple compounds as $CH_2=CH_2$ (λmax 180 mμ), $(CH_3)_2C=NCH_3$ (230 mμ), $CH_3N=NCH_3$ (373 mμ) etc.

** Including the electrons of the paired doublet of the electron-donating chromophore.

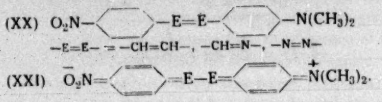
*** The cause of the shift was seen as the competition of the atoms for a link with the electrons ("the principle of electron competition").

**** The terms "ideal","limiting structure" used at that time should have shown that the formula being discussed was the generally accepted valency formula constructed on the additivity principle, in which changes resulting from the interaction of groups are not considered and which consequentely do not give the most precise representation of the actual structure.

***** This statement had in mind molecules made up of chromophoric groups showing absorption in the ultraviolet region, and was deduced from spectroscopic data. The absorption maxima for molecules made up of such chromophoric groups as C=C, C=O, C=N, NO_2, NH_2, C_6H_5-, $-C_6H_4-$, and so forth, calculated on the basis of additivity, i.e. for the case where no interaction was involved, should have lain similarly in the ultraviolet. Thus, for example, quinone, o-and p-nitroaniline should have been colorless compounds if no interaction between the groups was taking place, and the additivity rule was valid.

shift of the electrons shown in scheme (XIX), and the formation of a complex chromophoric system of the type B–K–A.

In accordance with the accepted modern theory the electron shifts in (XIX) should arise as a result of the interaction of the electron-donating (A) and the electrophilic (B) groups via the conjugated system K. The greater the electron-donating power* of the chromophoric group A: $N(CH_3)_2 > OH > OCH_3 > CH_3 > H$, and the electrophilic nature** of the chromophoric group B, the greater the shift of the structure (for example XX) towards the polar structure (XXI), the greater the charges δ– and δ+ (XII) and the more marked the displacement of light absorption towards the long-wave region should be. The experimental data confirm this [1].



The fact that the color and the spectrum of the three compounds mentioned (X), No. 8 (XI) are related to the presence of a similar π-structure (XIX) and to the interactions of the $B=NO_2$ and $A=N(CH_3)_2$ groups along the conjugated chain is clearly confirmed by the similarity of their absorption curves (Figure 4) and the similar magnitudes of ε for the long-wave band. This similarity in the spectral curves of all three compounds may be regarded as proof of the accuracy of the above ideas concerning the relationship between the color and spectrum and the electronic structure of the whole conjugated chromophoric system.

In the following Section 5 a theoretical approach to an explanation of the difference in color and spectra of azomethines of type (I) and type (II) is given, based on a more detailed analysis of the conditions for conjugation and electronic shift.

Notes on the problem of detailed electronic structural formulae (microstructures).*** The π-electron formulae (XIX), which gives a representation of the composition of the delocalized π-electron cloud and the forces acting in the molecule, are verysatisfactory for an understanding of the source and nature of the detailed electronic structure (microstructure) of the compounds examined. The microstructure of these compounds may be represented,

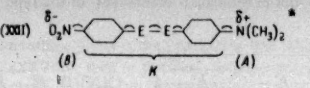
* The degree of electron-donating power may be measured by the basicity and characterized partly by the magnitude of the difference in dipole moment $\Delta\mu$ between the dipole moments for $A-C_6H_5$ and $A-CH_3$, and also by other methods.

** The electrophilic nature may be measured by determining the so-called "degree of electronegativity" (according to Pauling, Mulliken). It seems to us more suitable in accordance with the picture given earlier ([13], p. 111), to use in this case the term "degree of electrophilic nature" in place of the term "degree of electronegativity".

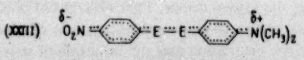
*** All forms of electronic formulae given above (footnote) as well as the generally accepted valency formulae, are constructed on the additivity principle. Atom and bond interaction are consequently not shown in them.

It is necessary to distinguish between the above "electronic formulae" and formulae in which an attempt is made by some means or other, involving greater or less detail, to reflect those details of the structure which appear as a result of the mutual influence of the atoms and bonds, the electron shifts and the breakdown of additivity. In place of the often-usedterm "electron formulae" it is appropriate to use another term for these formulae, namely–"detailed electronic structural formulae" or the shorter term microstructural formulae [15]. Contemporary formulae for electron shift and microstructure are, in reality, more precise versions of the earlier "formulae of state" (see, for example, [12], p. 323), expressed in the language of present-day symbols [19b].

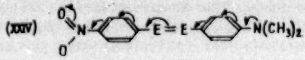
however, in a single formula by introducing into the structural formula, for example (XX), corrections indicating the delocalization of the separate electronic systems into a single conjugated system and the change in the distribution of the order of the bonds and the electron density. This can be represented using Thiele's symbol for conjugation (⌒), which has for long been used in detailed structural formulae [8,9,10,12] (see also: [14,15, 19b]) and the signs δ-, δ+ (XXII).

(XXII) 

Thomson (1914) and Robinson (1922) used a dotted line as the symbol for conjugation. The writing of such formulae, however, requires more time and they appear more complicated [16] (XXIII).**

(XXIII) 

In this case the conjugated structure (XXII) may be conditionally represented also by the formula (XXIV) as recommended in the report [19a].

(XXIV) 

Such formulae essentially show us, however, only the suggested mechanism and direction of the electron shift, whereas the chief requirement is to represent a definite microstructure. At the same time such formulae, in spite of their greater detail, particularly in the case of poly-condensed aromatic systems (see for example p. 341 [19b]), do not in general make it possible to represent the actual structure. They can be used only to represent one-directional shifts in the most simple systems (p. 161 [19b], [15]). Such formulae are in general unsuitable for dyes of the triphenylmethane series, such as crystal violet, for butadiene and stilbene, or even for benzene. Their use gives the impression that the actual structure is being represented and conceals the true state of affairs.

* For simplicity the double bond may also be left unchanged ⌒E=E⌒. Since all methods of representing the microstructure are after all only approximate and extremely arbitrary schemes, it is appropriate at this stage of the development of a microstructural formula for those compounds where the bands are not completely equivalent to simplify it as far as possible and preserve the resemblance to the classical structural formula which best expresses the properties of the compound. Thus the formula ...CH_2=CH⌒CH=CH_2... is more useful than ...CH_2‴‾CH‾‴CH‾‴CH_2... [16].

** From these considerations we must reject the representation of conjugation by a wavy line, introduced by Gebhard in 1910 [7] and afterwards widely used by V. Konig [18]. It is useful to reserve this symbol to represent partly heteropolar bonds.

5. The analysis of structural influences on color from the point of view of the interaction of two chromophoric systems—the complex electrophilic BK and the complex electron-donating AK : The theory of conjugated structure and the hypothesis of electron shift, as has been shown above, provide a route to the analysis of structural influences on the "color state" ("chromo-state"). This route was pointed out some years ago (see especially: [9], [12]). In a number of our own works [20,2,13,21] it has proved extremely useful to supplement this method by the use of a principle involving the breakdown of the molecular structure into polar chromophoric systems—the complex electrophilic (BK) and the complex electron-donating (AK). This principle was derived from a study of the problem of color in compounds with separated chromophoric systems of type (XXV) by comparing the color of these compounds with the color of molecular complexes of the type [BK + AK]* [13,22].

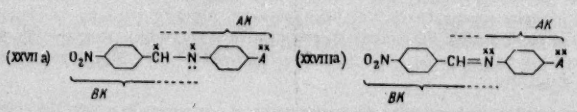
$$(XXV)\ \underbrace{(B-K-\overbrace{Q}^{\cdots}-\overbrace{K-A}^{AK}}_{BK}\quad (XXVI)\ \underbrace{\overbrace{B-K-A}^{AK},}_{BK}$$

where: B—electrophilic group (for example NO_2), A—electron-donating group [OH, OCH_3, N $(CH_3)_2$ etc.], K—conjugated system of double bonds (for example $-C_6H_4-$), Q—group breaking up the conjugation (for example $-CH_2CONH-$, $-CH_2-$, $-CH_2NH-$ etc.).

On the basis of a comparison of the effects (color, light absorption) observed on interaction of the above systems AK and BK in compounds with separated chromophoric systems of type (XXV) containing a general conjugated system, we have come to the conclusion that the principle of structure breakdown into polar chromophoric components BK and AK may prove useful also in a study of compounds with a conjugated system of type (XXVI) [23,24]. The usefulness of the concept of complex chromophoric systems AK and BK comes also from the following considerations: the analysis of the chromo-state in molecules of type B–K–Q–K–A and B–K–A, and in molecular complexes of type (BK + KA), from the standpoint of the principle of breakdown into separate chromophoric systems, leads us to the conclusion that the magnitude of the optical effect (bathochromic or hypsochromic) of the groups A or B depends not only on the structure of these groups but also on the structure of the system K to which the groups are linked. Thus we have in fact to deal not with the effect of A or B but with the effect of the system AK and that of the corresponding system BK, even in compounds with a conjugated system of the type B–K–A.

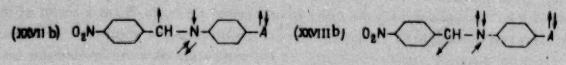
The dotted line in the curved brackets in (XXV) and (XXVI) should indicate that the group associated with AK or similarly with BK shows one or other modifying action on the chromophoric system AK or BK, strengthening or weakening the effect as a result of the changes in the electron-donating and the corresponding electrophilic properties. Thus, for example, it has been established that the increase in electron-donating power of the system AK by the addition of a second donor group in the para-position leads as a rule to a deepening of the color of the compound. The same action is shown by the increase in electrophilic nature of the BK system on introducing a second electrophilic group [20a,2,13].

In the present work we shall attempt to apply the above principle to the azomethines which we have studied, i.e. to conjugated compounds in which the –CH=N– group joining the benzene nuclei is capable of transferring the conjugation (XXVIIa). At the same time, however, in accordance with Sect. 1, we must take into account the fact that the nitrogen atom of the –CH=N– group, as a result of the presence of a free electron ("paired") doublet, is also able to become conjugated with the benzene ring of the aniline component [see formulae (IVa) and (IVb), and may thus to a certain extent be regarded as a component part of the electron-donating system AK, in fact as the principal donor in the absence of A (A=H) (XXVIIIa):

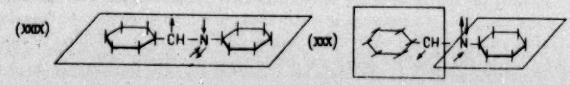


* I.e. complexes formed by the interaction of the same polar chromophoric systems BK and AK, but forming part of two different complex-forming molecules.

By using electron-spin formulae, we may represent the difference in structures (XXVIIa) and (XXVIIIa) by the more illustrative formulae (XXVIIb) and (XXVIIIb):



If the double bond of the azomethine group is the connecting link taking part in the formation of the general conjugated π-electron system (XXVIIb), then in this case, in accordance with the requirements of quantum-mechanical theory, both benzene nuclei, as shown in (XXIX), should be found in the same plane, while the electrons of the paired doublet of the N-atom do not take part in the formation of the conjugated π-structure*.



If, however, conjugation of the paired doublet with the right-hand benzene ring of the azomethine (XXVIIIb) takes place, then in this case the axes of the electron functions should be parallel to the electron function axes of the right-hand aniline nucleus and thus the benzene nuclei should lie in different planes (XXX), which will prevent any possibility of conjugation.** The interaction of the electrophilic and electron-donating system may then take place only by the interaction of their external fields. On the other hand the –CH=N– group, like the aldehyde group–CHO from which it is derived, may to a certain extent exhibit electrophilic properties and strengthen the electrophilic system BK.

In the molecule of the simplest representative of the azomethines–benzylideneaniline–both chromophoric systems BK and AK, like the connecting group–CH=N–itself, show extremely weak chromophoric properties; thus this compound is almost colorless. The α-maximum, which may be regarded as resulting from the interaction of these systems according to (XXX), is poorly-defined, while the most intense absorption band (the γ-band) lies in the same region (244 mμ) as the absorption band of the amino component (for benzylaniline, for example, λ max lies at 248 mμ). The introduction of the second much more powerful donating group $N(CH_3)_2$ into the aniline component in the para-position to the N-atom greatly increases the donating properties of this system,*** which also leads to a deepening of color in the corresponding compound. On the other hand, a second donor group in the paraposition relative to the nitrogen atom of the azomethine group lowers the tendency of the electron doublet of this nitrogen to become conjugated with the benzene nucleus of the aniline component according to (XXVIIIb) or (XXX) and in the same way increases the ability of the double bond of the–CH=N– group to become conjugated with the N $(CH_3)_2$ with the formation of a general, more extended π-electron system according to (XXVIIb) or (XXIX). As a result we observe a deepening of color in benzylidene-p-dimethylaniline (compound 2) not only in the solid state (an intense yellow color) but also in solution; the α-maximum of

* For simplicity, the arrows denoting π-electrons in the benzene nuclei in formulae (XXIX) and (XXX) are replaced by short lines.

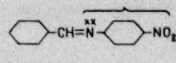
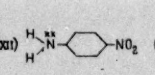
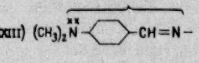
** Thus there arises the idea of two possible isomeric forms resulting from the geometrical conditions. If the idea of mutually perpendicular σ- and π-electron axes corresponds to reality, and is not merely a feature of the quantum-mechanical analysis of the electron cloud, then a special type of isomerism should exist: a geometrical isomerism connected with the difference in the electronic conjugation of the N-atom in the–CH=N and N=N– groups. In the case where delocalization of the three electrons in the nitrogen atom –$\ddot{N}$– proved possible, the existence of geometrical isomerism would be impossible, yet such a N-atom would still exhibit its donor properties and strengthen the electron-donating system AK.

*** As a result of the formation of a para- double donating system (see Section 1).

of this compound undergoes a marked bathochromic shift ($\Delta\lambda$ = +20 mμ) relative to the corresponding maximum of p-dimethylaminobenzylidenaniline (Figure 3, Curves 1 and 2, Figure 5, Curves 1 and 3, Table 2).

The introduction of a nitro group into the benzylidene part of the molecule, especially in the para-position relative to $-CH=N-$, greatly increases the electrophilic properties of the system BK, which leads to a deepening of color in compound 4 on comparison with the color of compound 1 (Table 2), as a result of the formation of an opposed system with two electrophilic groups in the para-position to one another, and also as a result of conjugation with the electron-donating system $=N-C_6H_5$. In the solid state an extra-molecular interaction between the powerful electrophilic system $O_2NC_6H_4CH=N-$ and even such a weak donor system as $=N-C_6H_5$ may also take place.

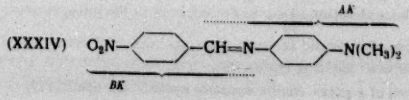
The introduction of a nitro group into the aniline part of the molecule enables the N-atom of the azomethine group to become conjugated with the nitro group via the benzene nucleus of the aniline component on account of the free electron doublet and in the same way leads to a lowering of its donor properties. The N-atom is, as it were, isolated from the left-hand benzylidene part of the molecule. As a result, an independent closed structure is formed, of the type B–K–A, which resembles p-nitroaniline in structure (see: XXXI and XXXII). This conclusion is confirmed by the similarity of the absorption curves of benzylidene-p-nitroaniline and p-nitroaniline (Figure 3, Curves 3 and 10). Thus the spectrum of benzylidene–p–nitroaniline may be regarded as the slightly modified p-nitroaniline spectrum with a slight hypsochromic shift resulting from the replacement of the hydrogen atoms of the amino group by the $C_6H_5CH=$ group and the decrease in electron shift.

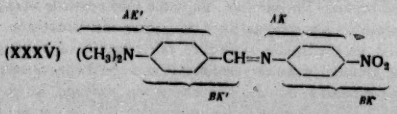
(XXXI)  (XXXII)  (XXXIII) 

A similar phenomenon is observed when the donor group $N(CH_3)_2$ is introduced into the benzylidene component, i.e. into the electrophilic part of the molecule (compound 3). Here again a closed system (XXXIII) is formed, also similar to a certain extent to the p-nitroaniline system (with the NO_2 replaced by the more weakly electrophilic $-CH=N-$ group). Thus the above compound has an absorption spectrum close to the spectra of compounds (XXXI) and (XXXII), and is less deeply colored than the corresponding para-isomer with the $N(CH_3)_2$ group in the aniline component (compound 2). In the latter a powerful double donating system is present, whose interaction with even such a weakly electrophilic system as $C_6H_5CH=N-$ leads to the production of a deeper color than in the previous case.

On the simultaneous introduction of both groups $-NO_2$ into the electrophilic component and $N(CH_3)_2$ into the electron-donating component (XXXIV)–we strengthen both systems–BK and AK–by the addition of groups of the same polarity in the para-position, i.e. in the position most favorable for the production of color. The interaction of these systems therefore gives a very large bathochromic effect; the a-maximum is shifted by +152 mμ and a compound with a deep red color is obtained.

We observe a much weaker effect with the position of the groups reversed. In this case we do not intensify, but in fact somewhat weaken, both the electrophilic nature and the electron-donating power of the appropriate components by introducing groups of opposite type. The compound (XXXV) is formed, constructed, as it were, from two systems which are to a certain extent independent, "closed" ("neutralized" or, in the nomenclature proposed by us, "syn-polarized") systems, which are less capable of interacting with one another. As a result, the maximum of the a-band undergoes a bathochromic shift much smaller than in the case of the isomer (XXXIV) (105 mμ instead of 152 mμ), and the compound has only a light red color whereas the isomer (XXXIV) has a deep red color

(XXXIV) 



Thus we come to the conclusion that an explanation for the deeper color of azomethines of type (I) is to be sought in the fact that the introduction of a donor group into the aniline part of the azomethine molecule, which may be regarded as the electron-donating system (AK), leads to an increase in this system's donor properties as a result of the formation of a para-double donating system; in a similar fashion the introduction of the NO_2-group into the benzylidene electrophilic part of the molecule (BK) leads to an increase in the electrophilic properties of the latter. As a result, two fairly powerful chromophoric systems of opposite character are formed, whose interaction, either via the –CH=N– group or directly via extra-molecular forces, leads also to the production of a deep color in the corresponding compounds.

The lighter color of azomethines of type (II) has been explained by the fact that when the position of the groups is reversed (i.e. on introduction of the donor group into the benzylidene and the NO_2 into the aniline component) two, as it were, independent parts are formed in the molecule, making up a system B–K–A, of which each part consists of a weaker electrophilic or electron-donating system (on comparison with the previous case).

EXPERIMENTAL

Since all the azomethines synthesized by us, with the exception of p-hydroxybenzylidene-p-nitroaniline, are described in the literature, we shall confine ourselves to a description of the methods of purification used for each specimen and a report of the melting points obtained by us and those given in the literature. A description of the method of preparing p-hydroxybenzylidene-p-nitroaniline is given, and more detailed data on its properties are listed (Table 3). The corresponding data for benzylidene-aniline (1), p-nitrobenzylideneaniline (4) and p'-nitrobenzylidene-p-aminophenol (6) have been given earlier [1].

TABLE 3

Specimen No.	Name of compound (for formulae see Table 1)	Purification of specimen by recrystallization	Melting point	
			found	from literature data
2	Benzylidene-p-aminodimethylaniline	Twice from methanol	99°	99° [25]
3	p-Dimethylaminobenzylideneaniline	Once from dilute ethanol and twice from methanol	100	100 [26]
5	Benzylidene-p-nitroaniline	Twice from a mixture of benzene and benzole (1:1) after washing the residue with ether	117–118	117–118 [27] 115 [28]
7	p'-Hydroxybenzylidene-p-nitroaniline [29]	Twice from dichloroethane	202–203	—
8	p'-Nitrobenzylidene-p-aminodimethylaniline	Twice from toluene	219.5–220	217 [30]
9	p'-Dimethylaminobenzylidene-p-nitroaniline	Twice from acetone	201–202	198–199 [31]

Preparation of p-hydroxybenzylidene-p-nitroaniline.* Equal quantities of p-hydroxybenzaldehyde and p-nitroaniline were mixed in a mortar and added to a wide test tube placed in an oil bath whose

* It is shown in the patent literature [29] that this material has been obtained by fusing equivalent amounts of p-hydroxybenzaldehyde and p-nitroaniline; it was not, however, isolated in a pure state, so that the melting point and analysis data are not given.

temperature had been previously raised to 150–155°. Heating was continued for about 1 hour during which the bath temperature was maintained between 130 and 135°, while the tube contents were stirred with a glass rod. On cooling, the mass which crystallized was recrystallized twice from dichloroethane. Brown-yellow crystals with m.p. 202-203° were obtained, readily soluble in alcohol, fairly readily in dichloroethane and toluene, with more difficulty in benzene. The material was easily hydrolyzed and could not therefore be crystallized from dilute alcohol or methanol. (Decomposition into the components was observed, which has to be taken into account in the spectroscopic work.) Our tests confirm the observation [32] concerning the easy hydrolysis of azomethines obtained from weakly basic aromatic amines.

Found %: N 11.66. $C_{13}H_{10}O_3N_2$. Calculated %: N 11.57.

The absorption spectra were measured by us using a Beckmann spectrophotometer. Ethyl alcohol (rectified) was used as solvent for most of the specimens, dichloroethane for specimens 5 and 7, 8 and 9. The dichloroethane was given a preliminary treatment with concentrated sulfuric acid, washed with sodium carbonate solution, then with water, dried with calcium chloride and redistilled.

The concentrations of the solutions used for the spectroscopic measurements were: $0.5 \cdot 10^{-2}$ and 10^{-4} M for compounds 2,3,5; $2 \cdot 10^{-2}$ and 10^{-4} M for compounds 7,8,9; 10^{-2} and 10^{-3} for specimen 1.

The reflection spectra were measured by us on an instrument constructed by E. V. Shpolsky. Details of the measurement have been given earlier [1]. The curves 2,3,5 (Figure 1) were measured on the Beckmann spectrophotometer.

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SUMMARY

1. A comparative study of the color, reflection spectra and absorption spectra of two series of azomethines of type(I) and type (II), where A =H, OH, $N(CH_3)_2$, has shown that azomethines of type (I) are more deeply colored than azomethines of type (II), both in solution and in the solid state. The theories of Diltey and Vitsinger [5] and of Smets and Delvaux [6] on the role of the azomethine group as the principal chromophore in these compounds do not explain the facts observed and are in error.

2. An explanation of the spectra has been given from the standpoint of conjugation and electron shift, making use of: a) the rule that bathochromic effect is related to the degree of electron shift; b) the principle that the molecular structure breaks down into polar complex chromophoric systems: the electrophilic BK and the electron-donating AK; c) the principle that the electron-donating properties are intensified by the introduction into the para-position of a second donor group A while the electrophilic properties are similarly intensified by the introduction of a second group B (contra-polarized systems).

3. On the basis of the similarity of the absorption spectra of the derivatives of benzylidene No. 8, stilbene (X) and azobenzene (XI), the azomethines of type (I) are regarded as examples of compounds of type B–K–A and the formation of a single conjugated chromophoric system with the two systems AK and BK.

4. Theories have been developed concerning the possibility that the groups –CH=N– and –N=N– take part in the conjugation not only by using the π-electrons of the double bond but also by using the electrons of the paired doublet of the N-atom, in the case where powerful electrophilic groups (NO_2) are present on the N-atom side.

5. The hypsochromic shift of color and absorption curves with azomethines of type (II) relative to azomethines of type (I) is regarded as the result of conjugation of the paired doublet of the N-atom of the azomethine group with the NO_2 and the consequent formation of two syn-polarized systems of type B–K–A (XXV) similar to the p-nitroaniline system. This conclusion is confirmed by the similarity of the absorption curves of benzylidene-p-nitroaniline and those of p-dimethylaminobenzylideneaniline, p-nitroaniline and benzylidenenitroaniline.

6. Some observations have been made on the subject of microstructural formulae.

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THE PREPARATION OF CHLORIDES AND ESTERS OF ARYLPHOSPHORIC ACIDS

CATALYTIC PHENOMENA IN THE REACTION OF PHENOLS WITH PHOSPHORUS OXYCHLORIDE

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Mixed esters of phosphoric acid of the type $ArOPO(OR)_2$ are usually prepared by the reaction of the appropriate phenoxides with dialkylchlorophosphates or of arylchlorophosphates with alcohols or alcoholates. The arylchlorophosphates are formed by heating phenols with the theoretical amount or with a slight excess of phosphorus oxychloride [1]; the reaction takes place at a fairly high temperature and leads to the formation of the mixture: $ArOPOCl_2$, $(ArO)_2POCl$, $(ArO)_3PO$. The latter point makes the second method of preparing alkylaryl phosphates less convenient. We have succeeded in showing, however, that by carrying out the reaction with a large excess of phosphorus oxychloride in the presence of a catalyst (KCl, NaCl and other salts) it is possible to obtain the monoarylchlorophosphates in almost quantitative yield. Thus, for example, if phenol is heated with an equimolecular amount of phosphorus oxychloride, as described by Freeman [2], monophenylchlorophosphate is obtained in 79.5% yield, while on heating 1 mole of phenol with 6 mole $POCl_3$ in the presence of 5 KCl the yield is 95.8%. In this reaction the potassium acts as a catalyst, since on heating phenol with a large excess of $POCl_3$, i. e. at the true boiling point of the latter (107°), practically no reaction takes place; if, however, a small quantity of KCl, NaCl or other salt is added to the reaction mixture evolution of hydrogen chloride commences immediately and the reaction proceeds smoothly to completion. The marked decrease in the reaction temperature enables one easily to obtain by this method 2,4,6-trinitrophenyl-2,4-dinitrophenyl and 4-nitrophenylchlorophosphates, which could not be prepared under the conditions usually adopted [3,9]. As a result, we have been able to synthesize in a fairly straightforward manner diethyl-4-nitrophenylphosphate (phosphacol), which is used in medicine as a myotic agent. The 4-nitrophenylchlorophosphate was obtained by us in 80-90% yield, while phosphacol was obtained in 77% yield by the reaction of the chloride with anhydrous ethyl alcohol according to the equation

$$O_2NC_6H_4OPOCl_2 + 2C_2H_5OH \longrightarrow O_2NC_6H_4OPO(OC_2H_5)_2$$

Scrader [4] obtained this compound by the reaction of sodium p-nitrophenoxide with diethylchlorophosphate or by the nitration of diethylphenylphosphate. Both methods have a number of disadvantages: the large number of stages, not all of which have good yields [for example, the preparation of $(C_2H_5O)_2POCl$ [5] etc.].

The catalysis of the reaction between phenols and $POCl_3$ by inorganic salts was confirmed by us for a number of cases: the various arylchlorophosphates were obtained. Nitrophenols, p-alkylphenols, dihydroxyphenols, their monomethyl esters and naphthols were used as starting materials. The corresponding diethyl esters were obtained from the chlorides by the action of absolute ethyl alcohol (Table 1).

The catalytic phenomena in the reaction of $POCl_3$ with phenols is of theoretical as well as preparative interest and was therefore studied further by us. The rate of the reaction

$$ArOH + POCl_3 + MeCl \longrightarrow ArOPOCl_2 + HCl + MeCl$$

was shown to depend on two factors: on the acidic properties of the phenol, i.e., on its dissociation constant, and on the metal whose salt was used as catalyst, i. e. on the nature of the cation. The kinetics of the reaction were determined by us from the quantity of hydrogen chloride separating during the reaction and measured by absorption in 1 N caustic soda solution. The NaOH solution was replaced by fresh material at definite time intervals and the quantity of hydrogen chloride determined by back-titration. The experimental results are shown graphically in the attached diagrams, in which the abscissae give the time in hours and the ordinates the percentage of hydrogen chloride evolved. The kinetics for the reaction of $POCl_3$ with phenols of different dissociation constant in the presence of NaCl are shown in Figure 1. It can be seen from a comparison of the curves that the rate of reaction increases with increasing dissociation constant of the phenols and is highest for picric acid. The obvious relation between the rate of reaction and the dissociation constant of the phenols, and the fact that inorganic salts are capable of dissociating in solution in $POCl_3$ [6], enable us to explain the mechanism of the catalytic action of NaCl in this reaction by means of the following equations:

$$ArO'H' + Na'Cl' \rightleftarrows ArO'Na' + HCl$$
$$ArO'Na' + Cl'POCl_2 \longrightarrow ArOPOCl_2 + Na'Cl'$$

The acidic properties of the phenols (for example picric acid) and the high ionizing power of $POCl_3$ [7] allow us to conceive the possibility of reaction (1), in which the equilibrium position lies over to the left. The phenoxide reacts instantly with the $POCl_3$ and thus allows reaction (1) to proceed to the right. Since hydrogen chloride is sparingly soluble in boiling $POCl_3$ and is removed from the reaction system, both reactions will proceed until all the phenol is used up. At the same time it must be pointed out that, as well as the dissociation constant, the position of the substituents in the phenol nucleus may be of some significance (spatial blocking). For example, o-nitrophenol ($K = 6.8 \cdot 10^{-8}$) reacts much more slowly than p-nitrophenol ($K = 6.1 \cdot 10^{-8}$).

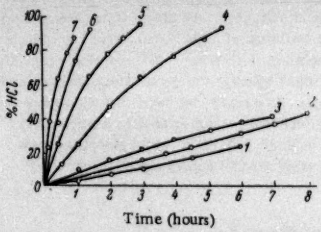

Fig. 1. Kinetics of the reaction of POC $_3$ with phenols (in the presence of NaCl).

1) guaiacol ($K = 1.71 \cdot 10^{-10}$, 2) 2-nitrophenol ($K = 6.8 \cdot 10^{-8}$), 3) phenol ($K = 1.3 \cdot 10^{-10}$), 4) 3-nitrophenol ($K = 5.0 \cdot 10^{-9}$), 5) 4-nitrophenol ($K = 6.1 \cdot 10^{-8}$; $9.4 \cdot 10^{-5}$); 6) 2,4-dinitrophenol ($K = 9.4 \cdot 10^{-5}$; $1.1 \cdot 10^{-4}$), 7) 2,4,6-trinitrophenol ($K = 1.6 \cdot 10^{-1}$).

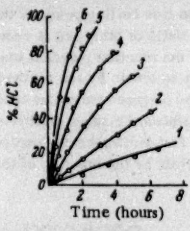

Fig. 2. Catalytic action of salts on the reaction of phenols with $POCl_3$.

1) $BaCl_2$, 2) NaCl, 3) KCl, 4) RbCl, 5) CsCl, 6) $FeCl_3$.

From the reaction mechanism indicated above it may be concluded that the increase in reaction rate should depend on the solubility of the salt in $POCl_3$, and that the greater this solubility, the greater the reaction rate. The observations made by us on the kinetics of the reaction of C_6H_5OH and $POCl_3$ (by the method described above) have shown that the addition of the chlorides of the 1st group elements brings about different increases in the rate of this reaction and that the reaction rate is least with NaCl, while CsCl brings about the greatest

TABLE 1

Sp. no.	Phenols	Catalyst	$ROPOCl_2$				$ROPO(OC_6H_5)_2$					
			yield (%)	% Cl found	% Cl calculated	Boiling point	yield (%)	% P found	% P calculated	Boiling point	d_4^{20}	n_D^{20}
1	o-$CH_3C_6H_4OH$	NaCl	91.0	31.38	31.55	118° (8mm)	52.0	12.39	12.71	119° (1.5mm)	1.1313	1.4812
2	p-$(CH_3)_2CHC_6H_4OH$	NaCl	88.5	28.18	28.06	145—146 (11mm)	83.0	11.51	11.39	174.5—175.5 (10mm)	1.0852	1.4770
3	p-C_2H_5—C(CH_3)(CH_3)—C_6H_4OH	KCl	89.3	25.35	25.30	155—159 (11mm)	76.1	10.53	10.33	144—146 (0.5mm)	1.0640	1.4838
4	p-$C_7H_{15}C_6H_4OH$	KCl	84.8	23.00	22.99	167—169 (1.5mm)	71.8	9.68	9.45	178—179 (2mm)	1.0328	1.4761
5	p-C_4H_9—C(CH_3)(CH_3)—C_6H_4OH	KCl	86.5	22.85	22.99	123—125 (0.5mm)	79.8	9.75	9.45	164—167 (1mm)	1.1380	1.4812
6	p-$C_9H_{19}C_6H_4OH$	KCl	89.0	21.20	21.07	167 (0.5mm)	77.6	8.90	8.71	181.5—184 (1mm)	1.0125	1.4765
7	p-$C_{12}H_{25}C_6H_4OH$	KCl	80.7	18.70	18.73	204—208 (1mm)	78.0	8.10	7.79	204—207 (0.5mm)	0.9673	1.4750
8	o-$CH_3OC_6H_4OH$	$FeCl_3$	89.0	29.30	29.46	120 (2 mm)	75.3	11.89	11.92	144 (1.5mm)	1.1872	1.4972
9	м-$CH_3OC_6H_4OH$	KCl	89.2	29.50	29.46	123—124 (1.5mm)	76.0	12.30	11.92	154—156 (1.5mm)	1.1750	1.4874
10	p-$CH_3OC_6H_4OH$	NaCl	88.3	29.35	29.46	118—120 (1.5mm)	55.0	12.28	11.92	148 (1mm)	1.1757	1.4865
11	o-$O_2NC_6H_4OH$	KCl	83.0	27.71	27.73	138—139 (1mm)	76.0	11.40	11.27	158—160 (1mm)	1.2761	1.4979
12	м-$O_2NC_6H_4OH$	NaCl	87.0	27.70	27.73	144 (1mm)	72.0	11.55	11.27	155—158 (0.5mm)	1.2745	1.4991
13	p-$O_2NC_6H_4OH$	NaCl	88.1	27.68	27.73	144 (1mm)	77.0	11.24	11.27	170—171 (1mm)	1.2782	1.5080
14	4-O_2N (2-CH_3) C_6H_3OH	NaCl	90.1	26.25	26.39		73.4	10.68	10.77	164—166 (0.5mm)	1.2516	1.5102
15	4-O_2N (2-CH_3O)C_6H_3OH	NaCl	88.2	24.81	24.91	169—171 (2mm)	65.0	10.08	10.20	187 (1mm)	1.2950	1.5141
16	α-Naphthol	KCl	85.0	27.13	27.2	138—140 (0.5mm)	71.9	11.28	11.07	151—154 (0.5mm)	—	1.5245
17	β-Naphthol	KCl	84.6	26.79	27.19	155—156 (1mm)	72.0	11.19	11.07	170 (1mm)	1.1792	1.5250
18	p-$C_6H_4(OH)_2$	KCl	85.6	40.85	41.27	212 (20mm)	73	16.60	16.24	184 (1mm)	1.2789	1.4725
19	м-$C_6H_4(OH)_2$	KCl	53	41.09	41.28	157 (1mm)						

increase. The difference in catalytic action of the various salts is readily seen from Figure 2, where the kinetics of the reaction of phenol with $POCl_3$ are given graphically. A comparison of the curves characterizing the reaction rate with Gutmann's data [6] on the solubility of these salts in $POCl_3$* at first sight confirms the suggestion made above. The difference in reaction rate obviously cannot be explained entirely by the solubility of the salts, since Gutmann determined the solubilities at 20°, whereas in our case, at the boiling point of $POCl_3$, the solubility relationships mayhave changed, apart from which the molar concentration of these salts are fairly close.** The reason for the different catalytic action of the different salts is not therefore quite clear, but it is obvious that the catalytic activity of the salts of the 1st group metals varies, and increases with increasing atomic number of the 1st group elements. The salts of elements of other groups also exhibit a catalytic action, for example, as we have confirmed: $BaCl_2$, $ZnCl_2$, $CoCl_2$, $FeCl_3$.

It should be noted that freshly distilled phosphorus oxychloride must be used in kinetic studies since the presence of hydrolysis products may change the reaction rate. We used twice-distilled phosphorus oxychloride (b.p.107° at 760 mm), while the phenol was vacuum distilled and had f.p. 40.4–40.6°. The other phenols and salts used were also carefully purified and dried.

EXPERIMENTAL

1. Preparation of phenyl chlorophosphate. a) (1 mole phenol + 1 mole $POCl_3$). A solution of 94 g phenol in 96 ml $POCl_3$ was boiled under reflux until the evolution of hydrogen chloride ceased, which took approximately 10 hours. During this time 35.9 g HCl was evolved. The mixture of chlorides obtained was vacuum distilled: at 106-111° (8-9mm) 168.3 g monophenyl chloropbosphate was distilled, at 111-120° – 6.0 g and at 120-188° – 21.3 g.

b) (1 mole phenol + 6.0 mole $POCl_3$). 5.0 g KCl was added to a solution of 94 g phenol in 549 ml $POCl_3$ and the mixture obtained heated under reflux until the evolution of hydrogen chloride ceased. Evolution of HCl stopped after 10 hours. The excess $POCl_3$ was distilled from the reaction mixture and the residue vacuum distilled. 202.1 g phenyl chlorophosphate distilled at 106-107.5° (7 mm), i.e. 95.8%.

Found %: Cl 33.59. $C_6H_5O_2PCl_2$. Calculated %: Cl 33.64.

2. Preparation of p-nitrophenyl chlorophosphate and reaction kinetics. 20.9 g (0.15 mole) p-nitrophenol and 83 ml (0.9 mole) freshly distilled phosphorus oxychloride were placed in a round-bottomed flask fitted with ground reflux condenser and boiled for 1.5 hours to confirm that no evolution of hydrogen chloride takes place and that the reaction does not proceed without the catalyst. 0.5 g NaCl was then added rapidly to the cooled reaction mixture and heating continued so that the mixture boiled vigorously. For the absorption of the hydrogen chloride evolved, the end of the spherical condenser was connected, via U-shaped tube filled with porcelain chips moistened with sulfuric acid, to a tube leading into a flask containing an accurately measured volume of 50 ml of 1 N NaOH. The NaOH solution was replaced by a fresh sample at definite time intervals and the quantity of HCl determined by back-titration. The results of the measurements are given in Table 2.

TABLE 2

Time of reaction (in hrs)	Amt. of 1N NaOH used in titration of evolved HCl at 0.5 hour intervals (in ml)	Amount of HCl evolved (%)	Catalyst
0.5	2.9		Without catalyst
1.0	0.5		
1.5	0.2		
0.5	37.46	25.04	0.5 g NaCl
1.0	37.69	50.27	
1.5	22.70	65.45	
2.0	17.31	77.15	
2.5	14.70	86.83	
3.0	12.10	94.81	
3.5	7.13	99.90	
4.0	2.90	—	
4.5	0.5	—	

*NaCl – 0.31 g/liter at 20°, KCl – 0.6 g/liter, RbCl – 0.87 g/liter, CsCl – 1.26 g/liter.

**NaCl – 0.00532 mole/liter, KCl – 0.00804 mole/liter, RbCl – 0.00719 mole/liter, CsCl – 0.00749 mole/liter.

When evolution of HCl had ceased, the excess phosphorus oxychloride was distilled under slightly reduced pressure from the reaction mass and the p-nitrophenyl chlorophosphate remaining (weight 37.9 g) was distilled at 2 mm; 33.8 g chloride distilled at 154-155° (88.0%)

Found %: Cl 27.68. $C_6H_4O_4NPCl_2$. Calculated %: Cl 27.74.

The determination of the reaction rates shown in Figures 1 and 2 was carried out similarly.

3. Preparation of diethyl-4-nitrophenyl phosphate (phosphacol). 33.6 g of 4-nitrophenyl chlorophosphate was placed in a round-bottomed flask fitted with a calcium chloride tube to prevent entry of moisture and 30 ml of anhydrous ethyl alcohol added slowly with cooling and stirring, and the mixture left until the following day. The excess of ethyl alcohol and the HCl were then distilled in vacuo from the reaction mass, the oily residue washed with water and sodium acetate solution, extracted with dichloroethane and dried. On removal of the solvent the diethyl-p-nitrophenyl phosphate obtained was vacuum distilled; 27.9 g (77%) distilled at 170-171° (1mm). After a second distillation the phosphacol had d^{20} 1.2782, n_D^{20} 1.5080.

Found %: P 11.24; N 5.05. $C_{10}H_{14}O_6NP$. Calculated %: P 11.27; N 5.09.

In the preparation of diethyl-p-nitrophenyl phosphate it is possible to use p-nitrophenyl chlorophosphate which has not been redistilled but from which the excess $POCl_3$ has been carefully distilled. The yield of ester in this case is approximately 70%, calculated from p-nitrophenol.

The chlorides and diethyl esters of the various aryl phosphoric acids given in Table 1 were prepared in exactly analogous fashion. The starting materials – alkylphenols with normal alkyl groups – were obtained by Clemmensen reduction of the corresponding hydroxyphenyl alkyl ketones. The hydroxyketones were obtained by the usual method – the condensation of acid chlorides with phenols in the presence of $AlCl_3$. The isoalkylphenols were obtained by condensing phenol with the corresponding alcohols in the presence of $ZnCl_2$ or $AlCl_3$ [8].

SUMMARY

The reaction of phenols with phosphorus oxychloride has been studied. It has been shown that phenols do not react with a large excess of $POCl_3$, which is evidently explained by the comparatively low reaction temperature; a large excess of $POCl_3$ does not allow the reaction mixture to be heated above 107-110°.

It has been shown that the chlorides of the elements of the 1st group of the periodic system act as catalysts in the reaction of phenols with $POCl_3$. The catalytic action of these salts increases with increasing atomic number of the element.

It has been shown that the catalytic activity of the salts depends to a large extent on the dissociation constant of the phenol used – the greater the dissociation constant the more rapid the formation of the aryl chlorophosphate. A mechanism of catalytic action of the salts in this reaction has been proposed.

It has been shown that by making use of the catalytic action of the chlorides of the elements of the 1st group of the periodic system it is possible to prepare easily and in good yield aryl chlorophosphates which cannot be obtained by heating the phenol with a slight excess of phosphorus oxychloride, for example, nitrophenyl chlorophosphate.

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THE ENZYMATIC HYDROLYSIS OF N-BENZOYL-O-PEPTIDES OF SERINE AND THREONINE

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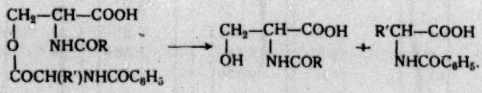
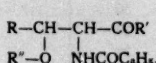
It has been shown earlier by us that the O-peptide (ester) link in N, O-diacetylphenylalanylserine and N-benzoyl-O-benzoylphenylalanylserine is broken by proteolytic enzymes [1].



Such behavior by the O-peptides of serine was not unexpected, inasmuch as, in accordance with contemporary theories, trypsin and chymotrypsin break not only amide, but also ester linkages [2]. The hydrolyzability of the ester link by proteolytic enzymes depends to a considerable extent on the structure of the substrate. The subject of these studies were, however, only the esters of the most simple alcohols with aminoacids or with purely carboxylic acids. The substrates studied by us differed in principle from those described in the literature, since the alcohol residues in them were those of β-hydroxyaminoacids. A compound of this type was subjected only once to hydrolysis by chymotrypsin. It was found [3] that the ethyl ester of N-benzoyl-O-benzoylphenylalanylserine was not decomposed by chymotrypsin. These results are in agreement with our observations that this peptide is not broken up by either trypsin or pancreatin [1]. The lability of the O-peptide link in serine O-peptides and its ability to be broken by enzymes point to the possibility of the formation of similar linkages in proteins and to the probable role of such peptides in biological processes. Thus, it is not impossible that the formation of complex protein compounds in protein systems takes place via a similar or analogous bond. The ease of migration of the peptide residue from nitrogen to oxygen and from oxygen to nitrogen [4] leads to the suggestion that the O-peptides may be intermediate compounds in the synthesis and hydrolysis of proteins. Thus it has been essential to extend the range of materials studied in reactions involving rupture of the O-peptide link in O-peptides of β-hydroxyaminoacids. With this aim, the present work was directed to the study of O-peptides not only of serine, but also of threonine and allothreonine of general formula:



where R = H or CH_3

R' = OH or $HNCH_3$,

R" = benzoylphenylalanyl, benzoylnorleucyl, benzoylvalyl.

Thus the "acyl residue" in the O-peptides was the benzoyl derivatives of aminoacids of the aromatic and aliphatic series, the "alcohol residue" —serine and threonine. The N-benzoyl-O-peptides of the hydroxyaminoacids and their derivatives listed were hydrolyzed by trypsin at pH 7.2. The hydrolysis of the O-peptides (Tests 1-7, Table 1) was carried out in 30% alcohol solution. The course of the hydrolysis was followed by titrating the carboxyl groups of the benzoylaminoacid liberated in the hydrolysis; in addition, the hydrolysis products were detected by paper chromatography. The studies showed (Figure 1 and Table 1) that the O-peptide link is broken by trypsin in N-benzoyl-O-benzoylphenylalanyl-D, L-threonine and N-benzoyl-O-benzoyl-norleucyl-D,L-threonine to an average extent of 40% after 2 hours. The rate of enzymatic rupture of the corresponding alloisomers

TABLE 1

Test No.	Name of O-peptide	Weight of O-peptide sample (mg)	Hydrolysis conditions: time (minutes)	Hydrolysis conditions: 0.1 N NaOH (ml)	Hydrolysis of O-peptide link (%)	Paper chromatography: R_f hydrolyzate	Paper chromatography: R_f "marker"
			15	0.20	7	0.33	Benzoyl-threonine 0.35
			30	0.44	16	0.68	Benzoyl-phenylalanine 0.67
1	N-Benzoyl-O-benzoyl-phenylalanyl-D,L-theonine	133.4 (with enzyme)	45	0.60	21	0.86	N-benzoyl-O-benzoylphenylalanyl-threonine 0.86
			60	0.71	25		
			75	0.81	29		
			90	0.84	30		
			105	0.87	31		
			120	1.00	35		
			135	1.09	39		
		110.5 (without enzyme)	135	—	—	0.87	N-benzoyl-O-benzoyl-phenylalanylthreonine 0.86
2	N-Benzoyl-O-benzoyl-phenylalanylallo-threonine	64.1 (with enzyme)	15	0.06	4.5		
			45	0.19	14		
			60	0.25	18		
			75	0.31	23		
			105	0.37	27		
			135	0.46	34		
3	N-Benzoyl-O-benzoyl-phenylalanylserine	142.8 (with enzyme)	10	0.27	10		
			20	0.38	15		
			30	0.47	18		
			40	0.59	23		
			50	0.66	26		
			60	0.75	29		
			70	0.82	32		
			80	0.89	34		
			90	0.97	38		
			100	1.03	40		
		118.6 (without enzyme)	10	0.03	2		
			30	0.08	5		
			80	0.11	7		

TABLE 1 (continued)

Test No.	Name of O-peptide	Weight of O-peptide sample (mg)	Hydrolysis conditions: time (minutes)	Hydrolysis conditions: 0.1 N N NaOH (ml)	Hydrolysis of O-peptide link (%)	Paper chromatography: R_f hydrolyzate	Paper chromatography: R_f "marker"
			20	0.24	9	0.81	Benzoylnorleucine 0.79
		112.1 (with enzyme)	30	0.44	17	0.90	N-Benzoyl-O-benzoylnorleucylthreonine 0.91
4	N-Benzoyl-O-benzoylnorleucyl-D,L-threonine		50	0.56	22		
			60	0.72	28		
			105	0.97	37	—	Benzoic acid 0.52
			135	1.11	44		
		112.3 (without enzyme)	10	0.02	0.6	0.91	N-Benzoyl-O-benzoylnorleucylthreonine 0.91
			60	0.06	2		
			135	0.17	6		
5	N-Benzoyl-O-benzoylnorleucylallothreonine	116.0 (with enzyme)	10	0.15	5.7	0.79	
			60	0.22	8	0.91	
			90	0.31	12		
			135	0.55	21		
6	N-Benzoyl-O-benzoylvalyl-D,L-threonine	116.8 (with enzyme)	90	0.03	1	0.82	Benzoylthreonine 0.34 Benzoylvaline 0.60 N-Benzoyl-O-benzoylvalylthreonine 0.79 Hydrolzate + benzoylvaline 0.63, 0.82
			135	0.09	3		
7	N-Benzoyl-O-benzoylvalylserine	96.5 (with enzyme)	90	0.09	4		
			130	0.12	5		

TABLE 2

Test No.	Name of O-peptide	Weight of O-peptide sample (mg)	Hydrolysis conditions: time (Hours)	Hydrolysis conditions: 0.1 M NaOH (ml)	Hydrolysis of O-peptide link (%)	Paper chromatography: R_f hydrolyzates	Paper chromatography: R_f "marker"
8	Methylamide of N-benzoyl-O-benzoyl-phenylalanyl-D,L-threonine	62.2 (with enzyme)	0.5	0.03		0.58	Hydrolzate + benzoylphenylalanine 0.58
			1	0.09	7		
			2	0.15	12		
			4.5	0.31	24		
			8	0.50	39		
			11	0.60	47		
9	Methylamide of N-benzoyl-O-benzoyl-phenylalanylallo-threonine	81.0 (with enzyme)	2	0.09	5	0.50	Hydrolyzate + benzoylphenylalanine 0.50
			4.5	0.21	13		
			11	0.31	19		
		47.8 (without enzyme)	2	0.03	3	—	Hydrolyzate + benzoylphenylalanine 0.50
			11	0.03	3		
		104.9 (with enzyme)	11	0.03	1	—	Hydrolyzate + benzoylnorleucine 0.65
10	Methylamide of N-benzoylnorleucyl-D,L-threonine	91.6 (without enzyme)	0.5	0.09	4	—	Hydrolyzate + benzoylnorleucine 0.65
			11	0.09	4		
11	Methylamide of N-benzoyl-O-benzoyl-valyl-D,L-threonine	84.3 (with enzyme)	2	0.06	3	—	Hydrolyzate + benzoylvaline 0.59
			11	0.09	4		

TABLE 3

No.	Name of O-peptide	Weight of O-peptide sample (mg)	Hydrolysis conditions		Hydrolysis of O-peptide link (%)
			Time (hours)	0.1 N Na OH (ml)	
12	Methylamide of N-benzoyl-O-benzoylphenylalanyl-D,L-threonine	163.3	0.5	0.12	3.5
			3.5	0.35	10
			9	0.77	22
			12	1.00	29
			15	1.16	34
			17	1.39	40
			20	1.54	45
		91.3•	20	0.06	3
13	Methylamide of N-benzoyl-O-benzoylphenylalanylallothreonine	128.2	4	0.26	9.5
			9	0.40	15
			10	0.47	17
			18	0.67	25
		65.1•	18	0.03	2
14	Methylamide of N-benzoyl-O-benzoylphenylalanylserine	60.5	0.5	0.20	6
			6	0.75	27
			13	1.18	35
			18	1.52	45
		17.2•	18	0.16	6.5
15	Methylamide of N-benzoyl-O-benzoylnorleucyl-D,L-threonine	118.7	18	0.13	5
		109.1	18		0
16	Methylamide of N-benzoyl-O-benzoylnorleucylallothreonine	77.4	18	0.22	13
17	Methylamide of N-benzoyl-O-benzoylnorleucylserine	102.5	4	0.24	10
			9	0.42	17.5
			12	0.69	29
18	Methylamide of N-benzoyl-O-benzoylvalyl-D,L-threonine	113.2	18	0.15	6
		109.7	18	0.16	6
19	Methylamide of N-benzoyl-O-benzoylvalylallothreonine	93.8	26	0.10	4.5
20	Methylamide of N-benzoyl-O-benzoylvalylserine	122.3	18	0.19	7

• Without enzyme.

(Tests 2 and 5, Table 1) is somewhat lower. In the absence of enzyme the hydrolysis of the ester linkage amounts to 7%; in these conditions autolysis of the enzyme is not observed. Benzoylthreonine, benzoylphenylalanine and some unhydrolyzed original O-peptide were detected by paper chromatography in the enzymatic hydrolyzates N-benzoyl-O-benzoylphenylalanyl-D,L-threonine, N-benzoyl-O-benzoylphenylalanylallothreonine.

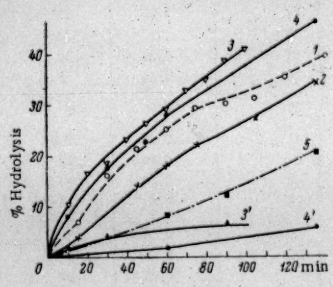


Fig. 1. Enzymatic hydrolysis of N-benzoyl-O-peptides of β-hydroxyaminoacids.

1) N-benzoyl-O-benzoylphenylalanyl-D,L-threonine; 2) N-benzoyl-O-benzoylphenylalanylallothreonine; 3) N-benzoyl-O-benzoylphenylalanylserine; 4) N-benzoyl-O-benzoylnorleucyl-D,L-threonine; 5) N-benzoyl-O-benzoylnorleucylallothreonine; 3',4') without enzyme

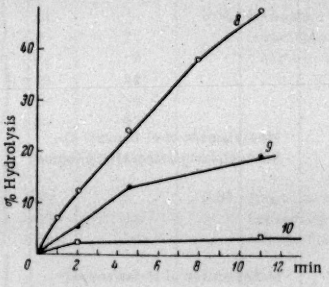


Fig. 2. Enzymatic hydrolysis of methylamides of N-benzoyl-O-peptides of threonine in aqueous alcohol medium.

8) Methylamide of N-benzoyl-O-benzoylphenylalanyl-D,L-threonine; 9) methylamide of N-benzoyl-O-benzoylphenylalanylallothreonine; 10) without enzyme.

Benzoylthreonine, benzoylnorleucine and N-benzoyl-O-benzoylnorleucylthreonine were found in the enzymatic hydrolyzates of N-benzoyl-O-benzoyl-norleucyl-D,L-threonine and N-benzoyl-O-benzoylnorleucylallothreonine. In the alkaline hydrolyzates of the above compounds only one substance was found: the unchanged O-peptide. No benzoic acid was found in any of the hydrolyzates; trypsin does not hydrolyze the O-peptide link in N-benzoyl-O-benzoylvalyl-D,L-threonine (Test 6) or N-benzoyl-O-benzoylvalylserine (Test 7) under the conditions described.

The hydrolysis of the methylamides of the O-peptides of D,L-threonine, allothreonine and serine (Tests 8-20, Tables 2 and 3) was carried out heterogeneously in 50% alcohol solution, and also in glycerol. The change in hydrolysis conditions compared with the O-peptides was made necessary by the low solubility of the methylamides in aqueous alcohol. In 50% alcohol, however, the enzyme is deactivated rapidly and a fresh sample of enzyme has therefore to be added after 4-5 hours (Figure 2). The enzyme retains its activity longer in glycerol solution, but the solubility of the methylamides in glycerol is also very small. In addition, the glycerol hydrolyzates cannot be chromatographed because of the presence of the high-boiling glycerol (Figure 3). The tests carried out showed that the ester link is broken in the methylamides of N-benzoyl-O-benzoylphenylalanyl-D,L-threonine (Test 8), N-benzoyl-O-benzoylphenylalanylallothreonine (Test9), N-benzoyl-O-benzoylphenylalanylserine (Test 14) and N-benzoyl-O-benzoylnorleucylserine (Test 17). The methylamides of N-benzoyl-O-benzoylnorleucyl-D, L-threonine (Test 10), N-benzoyl-O-benzoylnorleucylallothreonine (Test 16), N-benzoyl-O-benzoylvalyl-D,L-threonine (Test 18), N-benzoyl-O-benzoylvalylallothreonine (Test 19) and N-benzoyl-O-

benzoylvalylserine (Test 20) are not hydrolyzed by trypsin. The hydrolysis in 50% alcohol takes place somewhat more rapidly then in glycerol, and, other conditions being equal, the derivatives of D,L-threonine are hydrolyzed more rapidly than the corresponding derivatives of the allo-isomer. The hydrolysis of the O-peptide link in the methylamides is also confirmed from the chromatograms of the hydrolyzates. In the enzymatic hydrolyzates (Tests 9 and 8) benzoylphenylalanine is found; they do not contain benzoic acids or N-benzoyl-O-benzoylphenylalanylthreonine and give no reaction with periodic acid. Thus the ability to be hydrolyzed by enzymes is characteristic not only of O-peptides of serine but also of O-peptides of threonine and is probably a general property of O-peptides of β-hydroxyaminoacids. The lability of the O-peptide link evidently depends in the first instance on the aminoacid forming the acyl residue of the ester. Thus O-benzoylphenylalanyl-N-benzoylthreonine and O-benzoylphenylalanylserine and their methylamides are hydrolyzed by trypsin; the peptides and methylamides of peptides containing valine in their structure are, on the contrary, not hydrolyzed at all. The O-peptides of serine and threonine containing benzoylnorleucine in their structure are hydrolyzed by trypsin; of the methylamides corresponding to these peptides only that of serine is hydrolyzed.

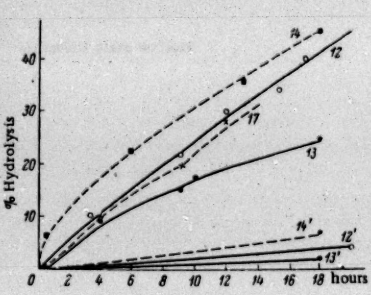


Fig. 3. Enzymatic hydrolysis of methylamides of N-benzoyl-O-peptides of β-hydroxyaminoacids in glycerol.
12) methylamide of N-benzoyl-O-benzoylphenylalanyl-D,L-threonine;
13) methylamide of N-benzoyl-O-benzoylphenylalanylallothreonine;
14) methylamide of N-benzoyl-O-benzoylphenylalanylserine;
17) methylamide of N-benzoyl-O-benzoylnorleucylserine; 12', 13', 14') action of alkali on the same amides.

EXPERIMENTAL

1. Enzymatic hydrolysis of the O-peptide link in N-benzoyl-O-peptides of D,L-and allothreonine and serine. The O-peptide sample was dissolved in 5 ml alcohol and neutralized with 0.1 N NaOH, and 2 ml phosphate buffer (pH 7.2), 5-6 ml water and 10 mg trypsin were added to the solution. The change in pH of the solution during hydrolysis was followed by potentiometric titration with a glass electrode (LP-4). The pH of the solution was restored to its original value by adding 0.1 N NaOH from a microburet. The tests were carried out at 32°. The hydrolyzates obtained as a result of the decomposition of the O-peptides of the β-hydroxyaminoacids were evaporated in vacuo at pH 5.5-6, the concentrated solutions obtained were diluted with alcohol and chromatographed on paper (approximately 0.1 mg material was used) in butanol solution saturated with 2N NH_4OH. After drying the chromatogram for 40 minutes at 135-140° it was developed with a solution of equivalent amounts of 1% KI, 0.5% $NaIO_3$ and 1% starch. To identify the spots obtained, a "marker" was run simultaneously, since the distribution coefficient of acylated aminoacids varies considerably with the type of paper and the concentration of the solution studied. The hydrolysis results are given in Table 1.

2. Hydrolysis of the O-peptide link in methylamides of N-benzoyl-O-peptides of threonine in aqueous alcohol. The hydrolysis conditions for the methylamides were similar to the hydrolysis conditions for the N-benzoyl-O-peptides described above. The only difference was in the concentration of the alcohol, which had to be increased to 50% because of the very low solubility of the materials studied. The hydrolysis results are given in Table 2.

3. Hydrolysis of the O-peptide link in methylamides of N-benzoyl-O-peptides in glycerol medium. The O-peptide methylamide sample was dissolved by heating in 8 ml glycerol and 2 ml phosphate buffer (pH 7.2), and 10 ml trypsin was added. No decomposition of the material takes place on heating an O-peptide in glycerol, since, for example, 85-90% of unchanged material can be isolated from the hydrolyzate of the methylamide of N-benzoyl-O-benzoylnorleucyl-D,L-threonine after 18 hours hydrolysis. The hydrolysis results are given in Table 3.

SUMMARY

It has been shown that the O-peptides of N-benzoylserine, N-benzoyl-D,L-threonine and allothreonine, and also their methylamides, can be broken down by trypsin.

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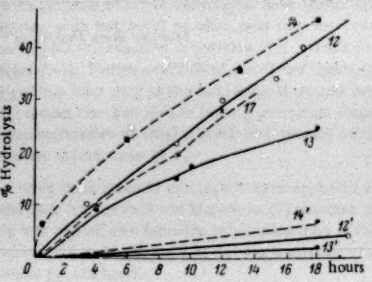
benzoylvalylserine (Test 20) are not hydrolyzed by trypsin. The hydrolysis in 50% alcohol takes place somewhat more rapidly then in glycerol, and, other conditions being equal, the derivatives of D,L-threonine are hydrolyzed more rapidly than the corresponding derivatives of the allo-isomer. The hydrolysis of the O-peptide link in the methylamides is also confirmed from the chromatograms of the hydrolyzates. In the enzymatic hydrolyzates (Tests 9 and 8) benzoylphenylalanine is found; they do not contain benzoic acids or N-benzoyl-O-benzoylphenylalanylthreonine and give no reaction with periodic acid. Thus the ability to be hydrolyzed by enzymes is characteristic not only of O-peptides of serine but also of O-peptides of threonine and is probably a general property of O-peptides of β-hydroxyaminoacids. The lability of the O-peptide link evidently depends in the first instance on the aminoacid forming the acyl residue of the ester. Thus O-benzoylphenylalanyl-N-benzoylthreonine and O-benzoylphenylalanylserine and their methylamides are hydrolyzed by trypsin; the peptides and methylamides of peptides containing valine in their structure are, on the contrary, not hydrolyzed at all. The O-peptides of serine and threonine containing benzoylnorleucine in their structure are hydrolyzed by trypsin; of the methylamides corresponding to these peptides only that of serine is hydrolyzed.



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TETRA-TERT-BUTOXYSILANE

M. G. Voronkov, A. N. Lazarev and A. K. Baigozhin

Until recently all attempts to prepare tetra-tert-butoxysilane $[(CH_3)_3CO]_4Si$ by the methods normally used for the synthesis of tetraalkoxysilanes have proved unsuccessful. Thus, for example, on reaction of silicon tetrachloride with tert-butyl alcohol only tert-butyl chloride and hydrated SiO_2 are found to be formed [1,2]. By carrying out this reaction in pyridine it is possible to replace two atoms of chlorine in $SiCl_4$ by tert-butoxy groups [2-4]. Further reaction of the di-tert-butoxydichlorosilane, obtained in this way, with tert-butyl alcohol in pyridine leads only to the formation of tri-tert-butoxychlorosilane [3,4]. The reaction of silicon tetrachloride with sodium tert-butoxide in boiling petroleum ether also gives the same compound [5,6].* Finally, in the transesterification of ethyl silicate with tertiary alcohols, no more than two tert-alkoxy groups can be introduced on to the silicon atom [8,9].

Only quite recently two reports have appeared in which the successful synthesis of tetra-tert-butoxysilane is described. Breederweld and Waterman [7] obtained this compound in 37% yield by heating tri-tert-butoxybromosilane with sodium tert-butoxide in a sealed tube at 220° for 10 hours. Hyde and Curry [10] synthesized tetra-tert-butoxysilane in 51.6% yield by boiling a solution of silicon tetrafluoride and sodium tert-butoxide in tert-butyl alcohol for 112 hours.

All attempts to prepare tetra-tert-butoxysilane by the reaction of tri-tert-butoxychlorosilane [5] or silicon tetrachloride [1] with sodium tert-butoxide have proved unsuccessful. In the particular case when tri-tert-butoxychlorosilane was heated with excess sodium tert-butoxide for 15 hours in a sealed tube, sodium tri-tert-butoxysilanoxide and hexa-tert-butoxydisilane were obtained instead of tetra-tert-butoxysilane.

In contrast to this we were able, as early as 1954, to prepare tetra-tert-butoxysilane in 47% yield by heating tri-tert-butoxychlorosilane with sodium tert-butoxide in toluene in an autoclave at 220° for 18 hours. It was also shown by us that tri-tert-butoxychlorosilane in turn could be prepared in 43% yield by the direct reaction of silicon tetrachloride with tert-butyl alcohol in the presence of pyridine in boiling toluene. The tetra-tert-butoxysilane was obtained by us as colorless crystals, stable in moist air, with m.p. 51.5°, distilling without decomposition at 222.0° (740 mm). It is interesting to note that Hyde and Curry [10] give a higher melting point for this compound (56.5-57°), while Breederweld and Waterman [7] give a lower one (48-49°). The infra-red absorption spectrum of tetra-tert-butoxysilane was studied in the region 1300-680 cm^{-1} in carbon disulfide solution and also in a finely powdered sample (by preparing a compressed disc from a mixture of powdered KBr and the material being studied [12]). **. The spectrum of crystalline $[(CH_3)_3CO]_4Si$ is no different from the spectrum

* $SiBr_4$ reacts similarly with sodium tert-butoxide [7].

** A spectrometer ISP-14b with rock-salt prism was used. A vacuum thermocouple constructed by B. P. Kozyrev was used to receive the radiant energy. The wavelengths of the absorption bands in the region studied were measured with an accuracy of ±0.03 μ. In the transmission curves given in the diagram the absorption of the solvent itself (which is very small in this region of the spectrum) was eliminated by measuring the absorption of a cell containing solution relative to that of a cell containing pure solvent. The spectra were studied at solution concentrations of from 6 to 20%; the thickness of the absorbing layer was approximately 0.02 mm.

of the carbon disulfide solution but gives finer detail. The values of the absorption band frequencies obtained are given in the Table.

Infrared Absorption Spectrum of tetra-tert-Butoxysilane

Frequency (cm^{-1})	Remarks
1300	Possibly 2 weak bands 1307 and 1298
1242	–
1192	–
~1115	Seen clearly only in the crystal spectrum
1063 }	Fully resolved only in cryst.
1053 }	spectrum
1027	–
910	Weak
831	–
705	–
690	Weak

The intense double band 1063,1053 cm^{-1} may be ascribed to the asymmetric bond vibration Si–O, as in other esters of orthosilicic acid [15]. The 1192 cm^{-1} band is related to the C–O bond and the 1027 cm^{-1} band to the O–C bond vibrations. The intense bands 1242 cm^{-1} and 705 cm^{-1} are possibly related to the vibrations of the C–CH_3 groups like the C–CH_3 and Si–CH_3 groups in polyalkylsiloxanes [13, 14]. The suggested interpretation is not final. Thus, for example, it may be suggested that the 1192 cm^{-1} frequency, like the 1242 cm^{-1}, is related to the vibrations of the tert-buty group [16]. The absorption spectrum of $[(CH_3)_3CO]_4Si$, obtained by Breederweld and Waterman [7] does not agree entirely with our data and is more complex. The spectrum is not given in full by the other authors[10] but the position of the Si–O band (9.37 μ) is in good agreement with the value obtained by us – 9.41 μ.

As a check on the purity of the material, the shortwave region of the infra-red spectrum of $[(CH_3)_3CO_4]Si$ was studied as well. The frequencies of the OH–and SiH–bond vibrations were not detected in the spectrum.

EXPERIMENTAL

Tri-tert-butoxychlorosilane. 170.0 g (1mole) of silicon tetrachloride was added dropwise with stirring to a mixture of 296.4 g (4 mole) of anhydrous tert-butyl alcohol with m.p. 25.5°, 316.4 g (mole) of dry pyridine and 300 ml of toluene distilled from sodium. The reaction mixture was then heated with constant stirring on a water bath for 10 hours (taking precautions to prevent entry of atmospheric moisture). The precipitate of pyridine hydrochloride was filtered off and was thoroughly washed with boiling toluene. 122.8 g of tri-tert-butoxychlorosilane with b.p. 198-202° (43.4%) was obtained by fractional distillation of the combined toluene solutions. After a second distillation it had:

B.p. 202-203° (760 mm), n_D^{20} 1.4033, d_4^{20} 0.928.
Found %: Si 9.87, 9.79; Cl 12.62, 12.67. $C_{12}H_{27}ClO_3Si$. Calculated for: Si 9.93; Cl 12.53.

Tetra-tert-butoxysilane. A mixture of 44.4 g (0.6 mole) of anhydrous tert-butyl alcohol, 250 ml of dry toluene and 11.5 g (0.5 mole) of metallic sodium was heated to boiling point with constant stirring for 6 hours. On cooling, the reaction mixture was freed from unreacted sodium and transferred to a steel autoclave of 0.5 liter capacity, into which 84.9 g (0.3 mole) of tri-tert-butoxychlorosilane was also added. The autoclave was heated for 18 hours at 220°. Fractional distillation of the reaction product on a column gave 10.0 g of unreacted tri-tert-butoxychlorosilane with b.p. 200-204°, n_D^{20} 1.4035 and 45.0 g tetra-tert-butoxysilane with b.p. 216-223°, yield 46.8% calculated from the original chlorosilane). After a second distillation it had m.p. 48.5-49°; b.p. 222.0° (760 mm); 97° (10mm); 68° (1mm); d_4^{20} 0.876, n_D^{20} 1.4028 (in the supercooled state), n_D^{50} 1.3902. After recrystallization from 96% alcohol it had a constant m.p. 51.5°. The infra-red spectra of the tetra-tert-butoxysilane before and after recrystallization were absolutely identical, which points to the absence of any reaction with the solvent on recrystallization and to the low concentration of impurity in the product before recrystallization.

Found %*: C 59.77, 60.10; H 11.30, 11.13; Si 8.68, 8.46. M 324.2, 326.0. $C_{16}H_{36}O_4Si$. Calculated %: C 59.95; H 11.32; Si 8.76. M 320.55.

* The microdetermination of C, H and Si was carried out by Yu. N. Platonov.

Literature data [7]: m.p. 48–49°, b.p. 92–95° (9mm), 60° (0.5 mm), [10] m.p. 56.5–57°; b.p. 105–105.5° (15 mm).

SUMMARY

The synthesis of tetra-tert-butoxysilane from tert-butyl alcohol and silicon tetrachloride via tri-tert-butoxychlorosilane is described.

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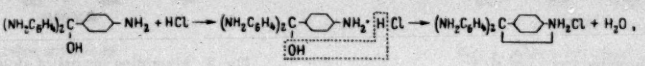
SPECTRA AND HALOCHROMISM

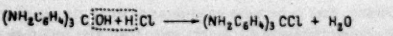
III. THE REACTION OF p-FUCHSIN, ANILINE BLUE AND THEIR CARBINOLS WITH ACIDS

V. F. Lavrushin and T. M. Shmaeva

In the process of the development of theories on the relation between color and structure in positively substituted triphenylmethane dyes, two different schools of thought have arisen. The representatives of one school defend the principle that the groups linked to the methane carbon atom are equivalent, while the representatives of the other school argue the opposite. The different views on the triphenylmethane dye structure have arisen to a great extent as a result of different treatments of the reaction by which they are formed. As early as the second half of the XIXth century E. and O. Fischer [1] and A. Rosenstiehl [2] put forward the two extreme points of view. The former regarded the formation of the dye as due to the reaction of the acid with an amino group.



while the latter considered that this reaction takes place at the carbinol hydroxy group.



These two viewpoints have since been reflected in the views of many workers and it cannot be said that one single point of view exists at the present time. At the same time much experimental material has accumulated over a considerable period in the study of the relation between color and the molecular structure of triphenylmethane dyes which makes it possible quite definitely to give preference to the reaction involving salt formation at the carbinol hydroxyl group. Salt formation at the carbinol group in unsubstituted arylcarbinols and in a number of their derivatives has been satisfactorily proved without any doubt in a great many studies devoted to the phenomenon of halochromism. Disagreement is found only in studies of the reaction by which dyes are formed from carbinols containing substituent groups of a basic character. In our opinion, this has arisen because certain workers base their ideas on an exaggerated view of the basic strength of the nitrogen-containing auxochromes and underestimate the basic strength of the carbinol group. This conclusion is confirmed by experimental studies specially carried out by us.

It is well known that in the reaction of strong acids with, for example, p-fuchsin, its color becomes yellow as a result of salt formation at the amino groups and their exclusion from the conjugation. No change in color is observed in the reaction of acetic acid, carbonic acid and boric acid; salt formation does not, therefore, take place at the amino groups with these weak acids.

We found that a colorless alcohol solution of the carbinol derived from p-fuchsin acquired the characteristic color of fuchsin by reaction with glacial acetic acid, carbon dioxide and boric acid. From measurements

of the absorption spectra of these solutions, curves were obtained which are identical with the curve for fuchsin itself, as can be seen from Figure 1. Since salt formation at the amino groups is excluded in this case, the only conclusion to which we can come is that the dye is formed by reaction at the carbinol group.

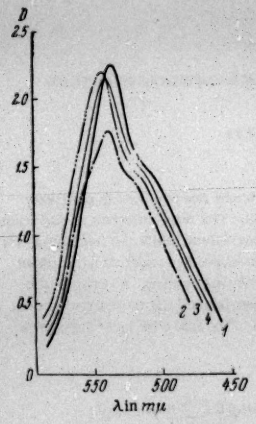


Fig. 1. Absorption spectra of alcohol solutions of 4,4',4"-triaminotriphenylcarbinol with CH_3COOH (1), H_2CO_3 (2) and H_3PO_4 (3); p-fuchsin in C_2H_5OH (4).

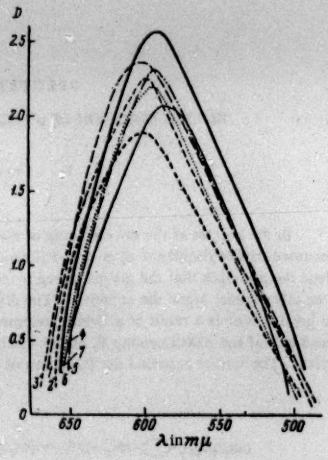


Fig. 2. Absorption spectra of alcohol solutions of aniline blue with 15% H_2SO_4 (1), 10% HCl (2), 75% H_3PO_4 (3), 90% CCl_3COOH (4), 75% $CH_2ClCOOH$ (5), glacial acetic acid (6); of aniline blue in C_2H_5OH (7).

To obtain more convincing data it became of interest to study the reaction of salt formation in a dye in which the nitrogen-containing auxochrome had a much lower basic strength than that of p-fuchsin.

As is known, increase in the number of aromatic radicals in amine molecules lowers their basic strength considerably, as a result of which, for example, the salts of diphenylamine are easily decomposed by water [3]; for further study we therefore chose the dye aniline blue with three diphenylamino groups, whose nitrogen atom has a very low basic strength.

By adding varying volumes of acids of different concentration to an alcohol solution of aniline blue we established that its color remains unchanged by the action of 15% sulfuric, 10% hydrochloric, 75% phosphoric, 90% trichloroacetic, 75% monochloroacetic and glacial acetic acids. From Figure 2 we see that their absorption curves have the same appearance as that of an alcohol solution of the dye, which points to the absence of salt formation by the auxochromes of aniline blue. The majority of the above strong acids change the color of p-fuchsin to yellow under the same conditions, which confirms that the basic strength of the auxochromes of aniline blue are indeed lower.

It next became of interest to discover whether a dye would be formed by the action of these acids on the carbinol derived from aniline blue.

It proved in the experimental tests that on addition of different volumes of strong acids to a colorless alcohol solution of the carbinol derived from aniline blue, the color of the dye was produced in all cases. In this way, as is shown in Figure 3, absorption curves identical with that of aniline blue were obtained.

We have already seen above that salt formation under these conditions does not take place at the auxochromes; formation of the dye therefore takes place by reaction with the carbinol group.

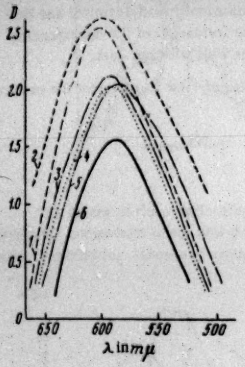


Fig. 3. Absorption spectra of alcohol solutions of 4,4',4"-triphenyltriaminotriphenylcarbinol with 15% H_2SO_4 (1), 10% HCl (2), 75% H_3PO_4 (3), 90% CCl_3COOH (4), 75% $CH_2ClCOOH$ (5); aniline blue in C_2H_5OH (6).

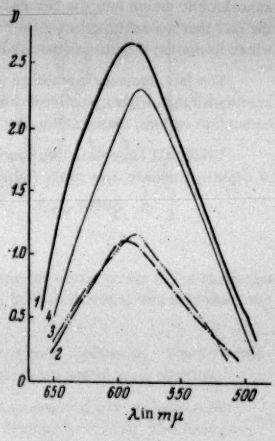


Fig. 4. Absorption spectra of alcohol solutions of 4,4',4"-triphenylaminotriphenylcarbinol with glacial acetic acid (1), H_2CO_3 (2), H_3BO_3 (3), aniline blue in C_2H_5OH (4).

Even greater interest was attached to an examination of the possibility of dye formation from the carbinol by the action of weak acids. With this aim the carbinol derivatives were treated with acetic acid, carbonic acid and boric acid. In this case also absorption curves were obtained which are similar to the aniline blue curve, as is seen from Figure 4.

Thus the data obtained by us in the study of the action of different acids on p-fuchsin and its carbinol, and, more especially, with aniline blue and its carbinol, show quite clearly that the formation of dyes from carbinols containing basic substituents takes place by salt formation at the carbinol group and involves the acid-base reaction: $Ar_3COH + HX \rightarrow Ar_3C^+ + X^- + H_2O$.

In a study of the phenomenon of halochromism in aromatic carbinols it has been established that the cause of the color produced by reaction with acids is to be found in the formation of a complex organic cation, for example, according to the following equation for triphenylcarbinol [4]:

$$(C_6H_5)_3COH + 2H_2SO_4 \rightleftarrows (C_6H_5)_3C^+ + 2HSO_4^- + H_3O^+.$$

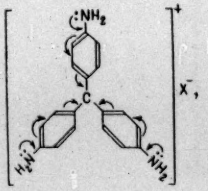
On the basis of the data on the halochromism of carbinols and the data obtained by us it is clearly seen that there is no difference in principle between the phenomenon of halochromism in aromatic carbinols and the reaction by which triphenylmethane dyes are formed from the carbinols, since in both cases carbonium salts are obtained. The only difference is that the former salts are more or less easily hydrolyzed, while the

latter are very stable and practically unhydrolyzed.

As early as 1940 P. P. Shorygin [5] wrote that "... from the halochromism theory these dyes are carbonium salts; the basic properties of the central C atom (the methane C) are evidently increased by the introduction of auxochromic groups into the benzene nucleus". And further: "... the quinoid theory cannot, however, explain the fact that malachite green gives not only mono-and diacid salts but also triacid salts (of a yellow color), whose formation is quite understandable from the theory of halochromism".

The fact, recently established by O. F. Ginsberg [6], that tetramethyldiaminotriphenylcarbinol and hexamethyltriaminotriphenylcarbinol dissociate in nitrobenzene solution with the formation of the corresponding carbonium cations, the former to the extent of 70% and the latter 90%, agrees well with our data.

Taking all these data into consideration, it is more useful from our point of view to represent the structure of triphenylmethane dyes in the following way [6-8]:



where the symbols in the formula are taken as indicating the ability of the atoms to become conjugated [9].

The superiority of this method of representing the structure of triphenylmethane dyes lies in the fact that it reflects accurately the direction of the influence of the substituents in the cation and corresponds fully to the generally accepted method of indicating this influence in more simple organic compounds [9]. Apart from which, this conjugated carbonium structure* for the triphenylmethane dyes agrees well with the conjugation in their cations, and moreover does not deprive the central carbon atom of the role which it plays as a result of its basic properties in the process of salt formation and production of color in the carbinols.

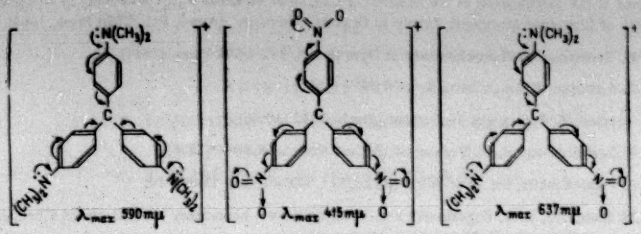
The cause of light absorption is the transfer of molecules from the ground state to an excited state [10], so that the smaller the energy difference between the excited and the ground state the longer the wavelength of the light absorbed by the material. As a result, a very important condition for the production of color is the presence in the molecule of an organic compound, of atoms or groups of atoms which raise the energy level of the ground state. A considerable raising of the energy level of the ground state takes place, for example, when a carbon atom in the molecules of organic compounds is transferred to the ionic state or forms a radical. As can be seen from Figure 5, the formation of free radicals and ions leads to absorption in the visible part of the spectrum [11]. From the fact that the free radicals corresponding to the triphenylmethane dyes are weakly colored [12], it follows that the most important condition for color in this type of dye is the formation of ions and the interaction of their auxochromes.

Since the formation of carbonium salts from tertiary aliphatic and alicyclic alcohols is always accompanied by color formation, we consider that the chromophore of the triphenylmethane dyes is the R_3C^+ carbonium ion, whose yellow color is deepened to an extent dependent on the nature of the conjugation in the groups linked to it.

The color of triphenylmethane salts depends on the conjugation within the cation, which is made up of several conjugated systems formed between the substituents in the benzene ring and the carbonium carbon.

* This term is adopted by us from a suggestion by B. A. Porai-Koshits.

The interaction of these systems is determined by the electrical character of the substituents and is a maximum when electron-donating and electron-accepting groups are present simultaneously in the cation:



The theory of the relationship between light absorption and the interaction of the groups in the molecules of organic compounds is not new and was put forward some time ago by A. E. Porai-Koshits, who used the concepts of oscillating atoms and groups [14].

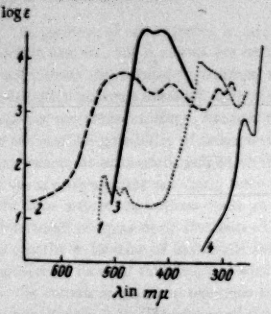


Fig. 5. Absorption spectra: 1) $(C_6H_5)_3C$; 2) $[(C_6H_5)_3C]^-$, 3) $[(C_6H_5)_3C^+]$ 4) triphenylcarbinol in C_2H_5OH.

Synthesis and purification of specimens. The p-fuchsin was purified by chromatographic adsorption on alumina.

The aniline blue was synthesized from p-fuchsin and aniline in the presence of benzoic acid [15]. The final purification was carried out by chromatography on alumina.

In conclusion we have to express our deep gratitude to A. N. Terenin for interest shown in the work and for valuable advice given.

SUMMARY

1. The behavior of p-fuchsin and aniline blue towards acids has been studied. It has been established that weak acids do not react with the auxochromes of p-fuchsin. The maximum concentrations of strong acids, at which they do not react with the auxochromes of aniline blue, have been found, and it has been established that no salt formation takes place at the auxochromes with weak acids.

2. It has been established that the formation of the dyes p-fuchsin and aniline blue from the corresponding carbinols takes place by reaction at the carbinol group.

3. Some considerations have been put forward on the use of a conjugated carbonium structure for triphenylmethane dyes and it has been concluded that their chromophore is the carbonium ion.

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* T: p. = C.-B. Translation pagination.

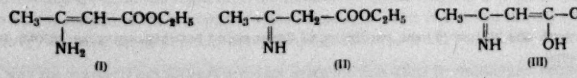
β-AMINOVINYL KETONES

VI. TAUTOMERISM OF ALKYL β AMINOVINYL KETONES

N. K. Kochetkov and Yanush Dombrovsky

In work previously published by A. N. Nesmeyanov and ourselves [1] we discovered that the refractive index of freshly distilled alkyl β-aminovinyl ketones, Alk–CO–CH = CH NH_2, increases rapidly to a definite constant value; when the distillation of the material with constant refractive index is repeated the phenomenon is reproduced exactly, and after a certain time the same maximum value of the refractive index is reached. The suggestion was made that a tautomeric change is taking place. The present work is devoted to a study of the nature of this phenomenon.

The problem of tautomerism in amino derivatives of β-dicarbonyl compounds arose as early as the end of the XIXth century, but it cannot yet be regarded as in any degree solved. There are many works, especially in the early literature, related to attempts to determine the structure of such materials on the basis of the structure of substitution products obtained from them. This did not lead, and as we now know, could not have led, to a solution of the problem, since, because of the possibility of a shift of the reaction center at the moment of reaction and also the possibility of tautomeric change under the reaction conditions, the structure of the starting materials cannot be accurately judged on the basis of the structure of the substitution products obtained from them. The works of this period are fairly fully covered in a survey contained in an article by Auwers and Susemihl [2]. In the same article the authors made an attempt to determine the structure of the amino derivatives of certain β-dicarbonyl compounds on the basis of refractometric data. They found that compounds of this type show a high specific exaltation of molecular refraction and dispersion, which have in addition approximately the same magnitude as those of their analogs with disubstituted nitrogen; since the latter can only have an enamino-structure, the authors ascribed an enamino-structure to the compounds with unsubstituted nitrogen, considering that they can contain only a low proportion of the imide form. In the case, for example, of the product of the reaction between acetoacetic ester and ammonia, this would mean the predominance of the aminocrotonic acid structure (I) over the acetoacetic ester ketimide structure (II).



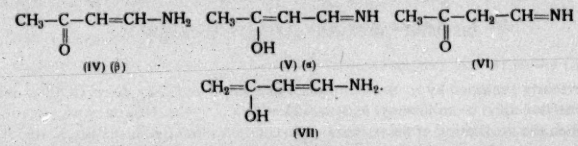
(I) (II) (III)

The possibility of the existence of another form with a conjugated bond system (III), suggested by Rugheimer [3], was rejected on the basis of general considerations concerning the absence of any tendency of the carbethoxy group to enolize, and, more especially, on the grounds that compounds of the type being considered do not give a reaction with ferric chloride [4], if sodium acetate, which prevents hydrolysis of amino compounds into ordinary β-dicarbonyl compounds, is previously added. These considerations were tacitly extended to the amino derivatives of β-diketones and hydroxymethylene ketones, and neither Auwers nor the majority of the other workers returned to the question of the possible existence of conjugated imido-enol structures (III or analogous structures). In cases where such materials were known in two isomeric forms they were given dis- and trans-structures. Only in very recent times has a work appeared, by American authors, in which all three of the structures analogous to formulae (I) (II) and (III) are taken into account, on the basis of the infra-red spectra of the products of the

reaction between acetylacetone and ethylene-diamine.*

We have convinced ourselves that the absence of a reaction with ferric chloride under the conditions described cannot be taken as proof of the absence of the imido-enol form of type (III), since sodium acetate prevents the reaction of enols in general with ferric chloride; we have discovered that in the presence of sodium acetate neither acetoacetic ester nor acetylacetone give any coloration. Thus the possibility of the existence of the imido-enol form of type (III) must again be taken into account.

The following structures are conceivable for the alkyl β-aminovinyl ketones, in particular methyl β-aminovinyl ketone, which we have studied:



(IV) (β) (V) (α) (VI)

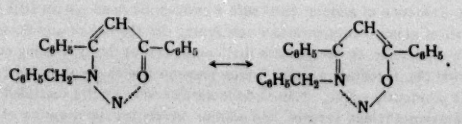
(VII)

Here formulae (IV), (V) and (VI) are analogous to formula (I), (II), and (III) given above, while formula (VII) represents enolization at the α'-methyl group. Apart from these cases, the possibility of cis-trans changes is not excluded, nor is the possibility of an association process, either of which could cause the change in refractive index of the material after distillation, which was described at the beginning of the article. To find out to what extent these last two processes are possible, we determined the energy of activation of the change from the kinetics of the change in refractive index. The energy of activation proven to be 15.5 kcal/mole. As is known, the activation energy of changes involving association is no greater than a few kcal/mole, while the energy of activation of cis-trans changes is usually not less than 25-45 kcal/mole; these two possibilities are therefore improbable. The value 15.5 kcal/mole obtained by us corresponds to the usual value for organic chemical reactions, including prototropic tautomeric change; thus, in our case, we are dealing with a prototropic tautomeric change, most probably involving a change from one of the structures (IV) to (VII) to another.

The idea of a possible reversible cis-trans isomerization does not bear criticism in this case for a further reason, namely that a similar change ought then to be observed for alkyl β-dialkylaminovinyl ketones of the type $R{-}CO{-}CH = CHNR_2'$, which in fact we have not observed. Thus it has remained for us to decide which of the four formulae given above correspond to the structure of the tautomers of methyl β-aminovinyl ketone.

We excluded the possible existence of the fourth of these structures (VII) on evidence provided by the behavior of compounds of corresponding structure. It turned out that tert-butyl β-aminovinyl ketone $(CH_3)_3C{-}COCH = CHNH_2$, which does not contain a hydrogen atom on the α'-carbon atom, also changes its refractive index

* In a paper by Cromwell and Watson [6] the possibility of "resonance" between enamino-ketone and imido-enol structures of the type



is considered.

A similar idea may be found in a paper by Culbertson [7].

after distillation (from n_D^{20} 1.5119 to n_D^{20} 1.5160); from which it follows that enolization in the direction of the methyl group cannot be the cause of this change. This conclusion is confirmed independently from methyl β-diethylaminovinyl ketone, $CH_3COCH = CHN(C_2H_5)_2$: if any tendency towards enolization in the direction of the methyl group existed, this compound would also change its refractive index on distillation, since the more volatile form always distils off preferentially at first; no such change in fact takes place. It is true that it may be taken a priori that a pure enol form with no tendency to change to the keto form is in fact distilling; this possibility is excluded, however, from the evidence of the infra-red spectra (the intense band of the C=O group is observed in the distillate, and the band of the OH group is absent).* From these facts the possibility of the existence of a form with structure (VII), in detectable quantities at least, must be rejected.

The question of whether the form with structure (IV) is present was decided by us from the refraction of freshly distilled methyl β-aminovinyl ketone and isobutyl β-aminovinyl ketone. As already mentioned, the refractive index and, naturally, other properties of an alkyl β-aminovinyl ketone change rapidly after distillation; it therefore became necessary to achieve an "aseptic" distillation, by which the distillate might be preserved for some time in its original condition and its refraction determined. Distillation in a quartz vessel did not lead to the the desired result; one form of the aminovinyl ketones evidently changes to the other at room temperature even in the absence of a catalyst. "Aseptic" conditions could only be achieved by using a low temperature; on distilling methyl β-aminovinyl ketone with the condenser cooled to −20° and the receiver at -25° we obtained a single tautomeric form of this substance (called the α-form) in a pure or practically pure state. It was obtained as a white crystalline mass, melting at 11-13°. The absorption spectra in the infra-red region gave proof of its purity (see below). By very careful work this α-form could be preserved for some time as a supercooled liquid and its refraction measured before crystallization began. The exaltation of the molecular refraction of the α-form EMR_D proved to be 2.95, the exaltation of the dispersion $E\sum_F - \sum_C = 186.5\%$ **. The exaltations of the refraction and dispersion obtained are so large that it is quite improbable that structure (VI), with no conjugated bond system, could correspond to the α-form. At the same time, it must be admitted that the second β-form too, which we have not yet succeeded in isolating in the pure state, cannot have the structure without a conjugated bond system (VI); in fact, the exaltations of the molecular refraction and dispersion of the tautomeric mixture obtained at room temperature have the still greater values $EMR_D = 3.626$ and $E(\sum_F - \sum_C = 204\%)$, so that, from the principle of additivity, the exaltations of the pure β-form are undoubtedly greater than 3.626 and the corresponding 204%.

In the same way we found that neither the α-nor the β-form of isobutyl β-aminovinyl ketone can have a structure analogous to (VI), since the α-form has the exaltation $EMR_D = 3.09$, while the tautomeric mixture has $EMR_D = 3.54$.

Having excluded the possibilites considered above, we may assume that in the case of the alkyl β-aminovinyl ketones studied by us we have to deal with imido-enamino tautomerism, which is simultaneously combined with keto-enol tautomerism by the mutual interconversion of structures (IV) and (V). This is confirmed by spectra of tautomeric mixtures of alkyl β-amino-vinyl ketones which contain frequencies corresponding to OH', NH_2, =NH, C=O, C=N and C=C; at the same time the frequencies of the NH_2 and C=O groups disappear almost completely from the spectra of the α-forms of these substances. This fact, taken in conjunction with the data considered above, allows us to assume that the α-form has the structure (V) and the β-form the structure (IV).

In this way the material put forward provides evidence that alkyl β-aminovinyl ketones exist as a tautomeric mixture of enamino-and amido-forms:

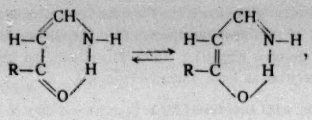
$$R{-}\underset{\underset{O}{\|}}{C}{-}CH{=}CH{-}NH_2 \rightleftharpoons R{-}\underset{\underset{OH}{|}}{C}{=}CH{-}CH{=}NH.$$

(β) (α)

* All the infra-red spectral data mentioned in this article were obtained by Ursula Dombrovskaya and Yu. A. Pentin in the molecular spectroscopy laboratory of the Moscow State University.

** All the exaltations are calculated relative to the structure $RCOCH = CHNH_2$; it is quite obvious that the exaltations relative to the $RCOCH_2CH = NH$ structures will be even greater; we did not calculate them, however, since there are no single data in the literature for the atomic refraction of imide nitrogen.

We are inclined to explain the unusually easy process of reversible isomerization of these two forms by the suggestion that both tautomeric forms of β-aminovinyl ketones have a chelate structure involving a hydrogen bond



so that the prototropic change boils down in reality to a change mainly in the electronic structure of the molecule and is related to a much smaller extent to the atomic nuclei. In this connection the magnitude of the activation energy of the change which we obtain (15.5 kcal/mole) acquires interest independently, since it characterizes the potential barrier of the hydrogen bond, which is the object of study of a number of workers [8].*

As is known, different solvents can displace the tautomeric equilibrium position in keto-enol systems to a marked degree, so that considerable interest was attached to a study of the influence of solvent in our case. We attempted to clarify this question on the basis of refractometric measurements. Because of the possibility of deviation from the principle of additivity, it is of course not to be expected that any quantitative results could be thus obtained, but nevertheless, taking into account the data obtained by Auwers and Wunderling [9], it was possible to hope that a conclusion might be reached concerning the direction of the equilibrium displacement by means of a comparison of the tautomeric mixtures with substances of corresponding structure. We have determined the apparent molecular refractions of methyl β-aminovinyl ketone in pyridine, dioxane and water. The refraction and dispersion of methyl β-aminovinyl ketone are decreased in pyridine and in dioxane, and have values intermediate between those of the α-form and the tautomeric mixture of this substance (Table 1, Nos. 1-6); it may be taken that this corresponds to an actual shift of the tautomeric equilibrium towards the α-form, since, firstly, the refraction in dioxane of tert-butyl β-diethylaminovinyl ketone, which is not capable of undergoing a tautomeric change (Table 1, Nos. 8,9) not only is not lowered, but, on the contrary, is somewhat raised, and, secondly, which is particularly convincing, a gradually decreasing change in solution density is observed when the tautomeric mixture from methyl β-aminovinyl ketone is dissolved in dioxane. The refraction and dispersion of methyl β-aminovinyl ketone are greatly increased in water; this cannot, however, be taken as a clear or sufficient indication of a shift of the tautomeric equilibrium towards the β-form, since the values of the refraction and dispersion of compounds of corresponding structure are also considerably raised in solvents containing hydroxyl groups (Table 1, Nos. 8,10,11,12). A more convincing indication of this shift is provided by the increase in intensity of the absorption band of the C-O group when methyl β-aminovinyl ketone is dissolved in water.

We were unable to find other solvents which were suitable from the point of view of chemical inertness, solvent power, low volatility and refractive index and density values (even with pyridine and dioxane the density had to be measured with an accuracy of 10^{-5}).

We have also studied the influence of temperature on the position of tautomeric equilibrium in methyl β-aminovinyl ketone using the refractometric method. We have found that when the temperature is increased the refraction of this compound falls at first and afterwards begins to rise slightly, whereas the dispersion falls regularly. At the same time it is known for almost all substances that on increasing the temperature the refraction and dispersion increase (the refraction on the average by 0.005-0.015%); we confirmed the latter point for methyl β-diethylaminovinyl ketone.

From this it may be taken that when the temperature is increased the equilibrium is slightly displaced towards the α-form of methyl β-aminovinyl ketone (Table 2, Figures 2 and 3).

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* Attention was drawn to this by Prof. Ya. K. Syrkin, for which we express to him our deep gratitude.

EXPERIMENTAL

Materials

The methyl β-aminovinyl ketone and isobutyl β-aminovinyl ketone were obtained by a method described earlier [1].

The tert-butyl β-aminovinyl ketone was obtained by a method similar to the above or by the action of an alcoholic solution of ammonia on hydroxymethylenepinacolin.

a) 400 ml of 25% aqueous ammonia was saturated with ammonia gas with simultaneous cooling of the solution to 5°;* then, without interrupting the current of ammonia, 14.6 g (0.1 mole) of tert-butyl β-chlorovinyl ketone was added dropwise over a period of 10 minutes with vigorous stirring and cooling.** The stirring was continued for 1 hour, after which the mixture was left for several hours in an ice bath. The solution was saturated with potassium carbonate and extracted with ether in an extractor for 4 hours; the ether was distilled off and the residue distilled in vacuo. Yield 9.1 g (71.6%), b.p. 76° (4mm).

Found %: C 66.43, 66.46; H 10.50, 10.57. $C_7H_{13}O$. Calculated %: C 66.10; H 10.30.

After distillation with condenser and receiver cooled with ice water the tert-butyl β-aminovinylketone had n_D^{20} 1.5119; after 10 hours the refractive index reached the constant value n_D^{20} 1.5160.

b) 4 g (0.031 mole) of hydroxymethylenepinacolin was added to a solution of ammonia (in 50 ml alcohol) saturated at 0°. After 4 hours, cooling was discontinued and the mixture left for 3 days at room temperature. It was dried with potassium carbonate, the alcohol distilled off and the residue distilled in vacuo. Yield 1.5 g (38%), n_D^{20} 1.5144.

The methyl β-diethylaminovinyl ketone was obtained by a method previously worked out by one of us [10]. A slight deviation in the refractive index and density values from those described had practically no significance in our case, since the material was being used for differential measurements.

The tert-butyl β-diethylaminovinyl ketone was obtained by the method of Auwers and Susemihl [2] from hydroxymethylenepinacolin and diethylamine. Yield 79%, b.p. 117° (3.5 mm). The density differed markedly from that described; it remained constant, however, after subsequent distillations.

The dispersion data for the materials obtained are given in Table 1.

Solvents. The bidistillate from a constantly operating plant was used.

Technical methyl alcohol was purified from acetone by boiling with furfural and alkali and afterwards distilled on an efficient column.

Commercially pure dioxane was boiled with hydrochloric acid, dried with solid potassium hydroxide and distilled on a fractionating column.

Commercially pure pyridine was dried for a year over solid potassium hydroxide and distilled on a fractionating column; 1/3 by volume was rejected at the start and end of distillation. The slight deviation of the solvent constants from those given in the literature (see footnotes to Table 1) are of no significance in our case in view of the differential nature of the measurements.

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* In the method published earlier it was recommended that the appropriate alkyl β-chlorovinyl ketone be added to an aqueous solution of ammonia, saturated at a temperature of from 0° to 3°; it subsequently turned out that the original chloroketone, if very pure, could freeze out at this temperature, which leads to a considerable reduction in yield; it is therefore better to carry out the reaction at a temperature of 5-7°; in this way the yield is not reduced.

** The tert-butyl-chlorovinyl ketone was kindly made available by I. Ambrush, to whom we wish to express our sincere gratitude.

TABLE 1

Refraction and Dispersion of β-Aminovinyl Ketones and their Solutions

No.	Substance	Percentage concentration	d_4^{20}	n_C^{20}	n_D^{20}	n_e^{20}	n_F^{20}	n_g^{20}
1	$CH_3COCH{=}CHNH_2$, M = 85.10, (*a*-form)	~ 100	1.0415 [2]	—	1.5638 [2]	—	—	—
2	The same	~ 100	1.0490 [3]	1.55996 [3]	1.56974 [3]	1.57945 [3]	1.59913 [3]	—
3	The same (tautomeric mixture)	100	1.02047	1.55723	1.56749	1.57722	1.59757	1.62772
4	The same in dioxane [4]	7.670	1.032462	1.43044	1.43300	1.43532	1.43984	1.44551
5	The same in pyridine [5]	6.369	0.984395	—	1.51248	—	—	—
6	The same in pyridine [6]	14.771	0.987239	1.51117	1.51654	1.52132	1.53077	1.54320
7	The same in water [7]	11.109	1.00635	1.35931	1.36214	1.36451	1.36939	1.37551
8	$(CH_3)_3CCOCH{=}CHN(C_2H_5)_2$, M = 183.29	100	0.89981	1.50582	1.51274	1.51924	1.53295	1.55324
9	The same in dioxane [8]	8.559	1.01970	1.42848	1.43101	1.43327	—	1.44325
10	The same in CH_3OH [9]	8.029	0.79976	1.34129	1.34333	—	1.34129	—
11	$CH_3COCH{=}CHN(C_2H_5)_2$, M = 141.21	100	0.93306	1.53004	1.53845	1.54637	1.56324	1.58800
12	The same in water [10]	11.757	0.99598	1.36013	1.36307	1.36558	1.37061	1.37738
13	$(CH_3)_2CHCH_2COCH{=}CHNH_2$, M = 127.18 (*a*-form)	~ 100	0.9680 [11]	—	1.5300 [11]	—	—	—
14	The same (tautomeric mix.)	100	0.9456	—	1.5221	—	—	—
15	$(CH_3)_3CCOCH{=}CHNH_2$, M = 127.18 (tautomeric mixture)	100	0.94227	1.50934	1.51600	1.52220	1.53516	1.55378

[1] The atomic refractions for the blue Hg line "*g*" (4358A) were obtained by interpolating Eisenior's data; they are: C 2.4645; H 1.1217; O 2.266; N^{I} 2.396; N^{III} 2.997; F 1.890.

[2] Temperature −15.4°.

[3] Temperature −22.1°.

[4] Dioxane d_4^{20} 1.03332, n_C^{20} 1.42048; n_D^{20} 1.42249, n_e^{20} 1.42427, n_F^{20} 1.42764, n_g^{20} 1.43161.

[5] Pyridine d_4^{20} 0.98246, — n_D^{20} 1.50961, — — —

TABLE 2

The Relationship Between the Refraction and Dispersion of Methyl β-Aminovinyl Ketone and Methyl β-Diethylaminovinyl Ketone and Temperature

No.	Compound	*t*	d_4^t	n_C^t	n_D^t	n_e^t	n_F^t
1	$CH_3COCH{=}CH-NH_2$, M = 85	20.00	1.02047	1.55723	1.56749	1.57722	1.59757
2	The same	38.65	1.00568	1.54686	—	1.56607	1.58593
3	"	59.10	0.98996	—	1.54525	—	—
4	"	60.37	0.98707	1.53524	1.54490	1.55391	1.57297
5	"	75.00	0.97493	1.52697	—	1.54522	1.56383
6	"	90.20	0.96282	1.51967	1.52873	1.53749	1.55554
7	$CH_3COCH{=}CH-N(C_2H_5)_2$ *M*=141.21 .	20.00	0.93174	1.52993	1.53841	1.54630	1.56311
8	The same	40.33	0.91701	1.52047	1.52885	1.53666	1.55305
9	"	75.13	0.88988	1.50418	1.51221	1.51968	1.53550

MR_C		MR_D		$MR_F - MR_C$		$MR'_g - MR_C$		EMR_D	$E(MR_F - MR_C)$	$E(MR_g - MR_C)$	$E(\Sigma_F - \Sigma_C)$ %	$E(\Sigma_g - \Sigma_C)$ %
calculated	found	calculated	found	calculated	found	calculated	found					
23.485	—	23.637	26.57	0.520	—	0.777	—	2.93	—	—	—	—
23.485	26.23	23.637	26.60	0.520	1.49	0.777	—	2.96	0.97	—	186.5	—
23.485	26.856	23.637	27.263	—	1.581	0.777	2.731	3.626	1.061	1.954	204.0	251.5
23.485	26.716	23.637	27.115	0.520	1.544	0.777	2.650	3.478	1.024	1.873	196.9	241.1
23.485	—	23.637	27.026	0.520	—	0.777	—	3.389	—	—	—	—
23.485	26.653	23.637	27.046	0.520	1.525	0.777	2.617	3.409	1.005	1.840	193.3	236.8
23.485	28.178	23.637	28.684	0.520	1.962	0.777	3.370	5.047	1.442	2.593	277.3	333.7
56.164	60.501	56.480	61.199	1.081	2.714	1.655	4.707	4.719	1.633	3.052	151.1	184.4
56.164	60.920	56.480	61.609	1.081	—	1.655	5.011	5.129	—	3.356	—	202.8
56.164	62.760	56.480	63.721	1.081	3.725	1.655	—	7.241	2.644	—	244.5	—
42.451	46.751	42.627	47.370	0.790	2.417	1.244	4.180	4.743	1.627	2.936	205.9	236.0
42.451	48.823	42.627	49.675	0.790	3.390	1.244	6.018	7.048	2.600	4.774	329.1	383.8
—	—	37.491	40.58	—	—	—	—	3.09	—	—	—	—
—	—	37.491	41.03	—	—	—	—	3.54	—	—	—	—
37.273	40.323	37.491	40.766	0.726	1.718	1.111	2.919	3.275	0.992	1.808	136.6	162.7

[6] Pyridine d_4^{20} 0.98253, n_C^{20} 1.50497, n_D^{20} 1.50963, n_e^{20} 1.51371, n_F^{20} 1.52155, n_g^{20} 1.53147.

[7] Water d_4^{20} 0.99823, n_C^{20} 1.33141, n_D^{20} 1.33321, n_e^{20} 1.33459, n_F^{20} 1.33734, n_g^{20} 1.34030.

[8] Dioxane d_4^{20} 1.03332, n_C^{20} 1.42038, n_D^{20} 1.42245, n_e^{20} 1.42421, n_F^{20} 1.42756, n_g^{20} 1.43158.

[9] CH_3OH d_4^{20} 0.79125, n_C^{20} 1.32750, n_D^{20} 1.32903, — n_F^{20} 1.33275, —

[10] Water d_4^{20} 0.99823, n_C^{20} 1.33134, n_D^{20} 1.33318, n_e^{20} 1.33466, n_F^{20} 1.33730, n_g^{20} 1.34038.

[11] Temperature −12.3°.

n'_g	MR'_C		MR'_D		MR'_e found	$MR'_F - MR'_C$		$E(MR_F - MR_C)$	$E(\Sigma_F - \Sigma_C)$ %
	calculated	found	calculated	found		calculated	found		
1.62772	23.485	26.856	23.637	27.263	27.646	0.520	1.581	1.061	204.0
1.61501	23.485	26.831	23.637	—	27.607	0.520	1.566	1.046	201.2
—	23.485	—	23.637	27.190	—	0.520	—	1.046	—
1.60100	23.485	26.853	23.637	27.255	27.628	0.520	1.556	1.036	199.2
—	23.485	26.836	23.637	—	27.608	0.520	1.549	1.029	197.9
—	23.485	26.872	23.637	27.266	27.650	0.520	1.537	1.017	195.6
1.58795	42.451	46.809	42.627	47.434	48.010	0.790	2.419	1.629	206.2
1.57744	42.451	46.849	42.627	47.480	48.055	0.790	2.431	1.641	207.2
1.55930	42.451	47.002	42.627	47.632	48.216	0.790	2.439	1.649	208.7

The Kinetics of Conversion of the α-form of Methyl β-Aminovinyl Ketone

The relation between the initial rate of conversion of the α-form of methyl β-aminovinyl ketone and the temperature was studied to determine the energy of activation. The rate of conversion was measured by the change in refractive index. The α-form was isolated as follows: methyl β-aminovinyl ketone which had been previously twice distilled was distilled from a Claisen flask fitted with a fractionating column whose outlet tube was cut short and sealed directly to the sleeve of a condenser. A stream of alcohol cooled to -20° was passed through the sleeve, while the receiver was cooled to −25°. During the distillation the air entering the capillary was dried over alkali; after the distillation, similarly, dried air was admitted to the apparatus.

A drop of material was then placed on the prism of an Abbe refractometer in an air thermostat, while shaking was avoided (to prevent the onset of crystallization).

The speed of conversion is subject to the catalytic influence of traces of impurities which the methyl β-aminovinyl ketone may contain in spite of careful purification. In different, independent experiments the initial rates of conversion vary considerably among themselves; in spite of this, however, the energy of activation remains practically constant. Other factors (adsorption of gases from the air, catalytic action of the prism, etc.) had no influence on the rate of conversion; within a given series of experiments (material from the same distillation) the initial rate of conversion showed very good reproducibility. Measurements were carried out in three series: 1st 10.0, 15.1 and 30°, 2nd 20.0, 25.1, 30.3 and 35°; 3rd 6.9, 12.1, 17.3, 25.0, 27.5 and 31.2°. The results of the experiments are given in Figure 1 in the form of the relationship between $\ln W_0$ and $1/T$.

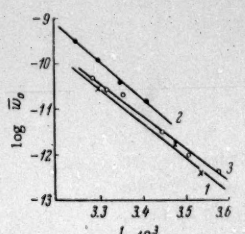

Fig. 1. The relationship between the logarithm of the apparent initial rate of conversion of the α-form of methyl β-aminovinyl ketone and temperature.
1−E = 15.8 kcal/mole, 2−E = 16.2 kcal/mole 3−E = 14.4 kcal/mole.

Refraction of the α-form of Methyl β-Aminovinyl Ketone and Isobutyl β-Aminovinyl Ketone

The preparation of the α-form of methyl β-aminovinyl ketone is described in the preceding section. After distillation the material was carefully placed in the prism cell of a Pulfrich refractometer situated in an air thermostat −a refrigerator fitted with the necessary windows and sleeves. Some experiments were carried out using an Abbe refractometer. The temperature within the air thermostat was maintained within ± 1°, while the temperature of the refractometer prism was controlled within ± 0.05° using a Bobzer thermostat with an extra control resistance of 250 Ω fitted to the heater. For the density determinations the material was distilled, under the conditions described, directly into a pyknometer of 14 ml capacity which was then placed in a thermostatically controlled Bunsen vessel in an air thermostat; after 15 minutes the volume of the liquid was determined, using a cathetometer, from the position of the meniscus between the marks engraved on the neck of the pyknometer.

The results of the measurements are given in Table 1 (Nos. 1,2 and 13).

Analysis of Experimental Errors

Density. The radius of the pyknometer neck $r \approx 4$ mm. The accuracy of the cathetometer readings ± 0.05 mm. For the four readings required (mark and meniscus for the calibration and the density determination) the maximum error is ± 0.2 mm. A cylinder of this height has a volume $v = 0.02 \cdot 3.14 \cdot 0.4^2 \approx 0.01$ cm^3, which gives a maximum error for the density of $\pm 7 \cdot 10^{-4}$. The error due to temperature variation (± 0.05°), and the error of weighing are of the order of 10^{-5} and are neglected. The densities, like all those quoted later, are reduced to vacuum.

Refractive index. The absolute values of the refractive indices were determined in both refractometers with an accuracy of $\pm 1 \cdot 10^{-4}$. The Pulfrich refractometer IRF-23 is able to determine the difference $n_1 - n_2$ with an accuracy of $\pm 2 \cdot 10^{-5}$, but because of the temperature variations the accuracy falls to approximately $\pm 6 \cdot 10^{-5}$. The temperature correction factors of the prism were taken into account in the determinations of the

refractive indices at temperatures other than 20°.

Using these data and the well-known formula [11] we obtained for methyl β-aminovinyl ketone

$$\nabla MR_D \approx MR_D \left[\frac{6n}{(n^2+2)(n^2-1)} \cdot \nabla n + \frac{\nabla d}{d} \right] \approx \pm 0.02 \text{ ml/mole}$$

and for isobutyl β-aminovinyl ketone $\nabla MR_D \approx \pm 0.04$ ml/mole.

The error introduced into the determination of the dispersion from the inaccuracy of the density measurement has a small value of the second order and is neglected. Thus for methyl β-aminovinyl ketone we have approximately

$$\nabla (MR_F - MR_C) \approx 0.5 \nabla (\Delta n) \left[\frac{MR_F \cdot 6n_F}{(n_F^2+2)(n_F^2-1)} + \frac{MR_C \cdot 6n_C}{(n_C^2+2)(n_C^2-1)} \right] \approx \pm 0.0023 \text{ ml/mole}$$

and for the specific dispersion

$$\nabla E(\Sigma_F - \Sigma_C) \approx \frac{\nabla (MR_F - MR_C) \cdot E(\Sigma_F - \Sigma_C)}{E(MR_F - MR_C)} \approx \pm 0.4\%.$$

The refraction and dispersion of the tautomeric mixtures were determined with greater accuracy. The density was measured with an accuracy of $\pm 5 \cdot 10^{-5}$ (pyknometer of 10 ml capacity with narrow neck, temperature ± 0.01°, calibrated set of weights) and the difference n_1-n_2 with an accuracy of $\pm 2 \cdot 10^{-5}$ [the refractive indices were measured for the red (C) and blue (F) hydrogen lines, the sodium line (D) and the green (e) and violet (g) mercury lines]. Thus for methyl β-aminovinyl ketone we have: $\nabla MR_D \approx \pm 0.005$ см³ and $\nabla E(\Sigma_F - \Sigma_C) \approx \pm 0.2\%$, and for isobutyl β-aminovinyl ketone $\nabla MR_D \approx \pm 0.009$ ml/mole.

From this it can be easily seen that the observed difference in refraction and dispersion for methyl β-aminovinyl ketone and its tautomeric mixture is 30 times greater than the maximum experimental error. In the case of isobutyl β-aminovinyl ketone the analogous difference in refraction is 9 times greater than the experimental error.

The Refraction of Aminovinyl Ketone Solutions

The differences in refractive indices were measured on a Pulfrich refractometer with an accuracy of $\pm 2 \cdot 10^{-5}$. The density of the solutions of methyl β-aminovinyl ketone in dioxane and pyridine was measured using two pyknometers by the differential method described by Skarre, Demidenko and Brodsky [12]. The pyknometers had a smaller capacity (30 ml instead of 50) and a somewhat wider neck (0.65 mm instead of 0.5 mm) than the pyknometers used in the work referred to; thus the accuracy of Δd was $\pm 5 \cdot 10^{-6}$ instead of $\pm 1 \cdot 10^{-6}$, which was sufficient for our purposes. A precision thermostat TP-1 made by "Platinum Instruments", with an accuracy of ± 0.001°, and a KM-10 cathetometer measuring the distances between the marks and the menisci with an accuracy of ± .01mm, were used. The density of the other solutions and the density of all the solvents were measured using one of the pyknometers described, giving an accuracy for Δd of $\pm 2 \cdot 10^{-5}$.

The maximum errors in the apparent refraction, calculated according to the formula [13]:

$$\nabla MR_D \approx \frac{1000}{C} \left[\frac{6n_0}{(n_0^2+2)^2} \nabla (\Delta n) + \frac{n_0^2-1}{(n_0^2+2)d_0} \nabla (\Delta d) \right]$$

(where C—concentration in mole/liter, and index "zero" refers to solvent) had the values: from 0.007 to 0.02 ml in tests 4-7,12 (Table 1) and 0.03 ml in tests 9,10. The maximum errors in the dispersion (in absolute figures) were 1-2% in tests 4,6,7 and 4% in tests 9,10 and 12.

As already pointed out, a gradually decreasing change in solution density takes place when methyl β-aminovinyl ketone is dissolved in dioxane. In 3 days the volume of 30 ml of 7.7% solution increased by 0.03 ml and then became constant; in spite of the small magnitude of this difference, it is 1200 times greater than the experimental error (reading meniscus height with cathetometer).

Methyl β-aminovinyl ketone gradually decomposes in aqueous solution: approximately $\frac{2}{3}$ of the initial quantity of ketone decomposes in 2 weeks; the refractive index and the density were therefore measured immediately after the solution was prepared.

Relationship between the Refraction of Aminovinyl Ketones and Temperature

The measurement of the densitites and refractive indices was carried out in an air thermostat. After the determination of the refraction at a high temperature the materials were cooled and a check was made to find whether their constants had changed as a result of decomposition. With rapid work the constants of the materials remained the same within the limits of experimental error. The measurements were carried out in the range 20-90°; the results are given in Table 2 and Figures 2 and 3. In Figure 2 data obtained for the most distinct green mercury line e are used; in Figure 3 dispersion data for the blue and red hydrogen lines $E(\Sigma_F - \Sigma_C)$ are used.

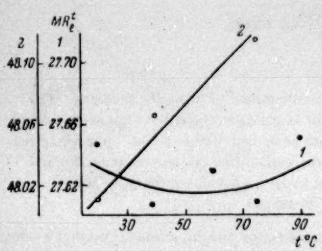

Fig. 2. The relationship between the refraction MR_e of methyl β-aminovinyl ketone (1) and methyl β-diethylaminovinyl ketone (2) and temperature.

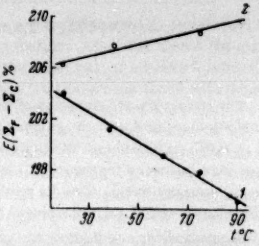

Fig. 3. The relationship between the dispersion $(\Sigma_F - \Sigma_C)$ of methyl β-aminovinyl ketone (1) and methyl β-diethylaminovinyl ketone (2) and temperature.

The temperature in the Bunsen vessel and in the refractometer was maintained with an accuracy of ± 0.05°. The density was determined in a pyknometer of 10 ml capacity with an accuracy of $\pm 1 \cdot 10^{-4}$; the absolute values of the refractive indices were measured with an accuracy of $\pm 1 \cdot 10^{-4}$, their difference with an accuracy of $\pm 6 \cdot 10^{-5}$. Thus, from the formulae given above, we have for methyl β-aminovinyl ketone (from data for the intermediate temperature 60°, Table 2, No. 4): $\nabla MR_e \pm 0.007$ ml/mole and $\nabla E(\sum_F - \sum_C) \approx \pm 0.5\%$; for methyl β-diethylaminovinyl ketone (from data for 40°, Table 2, No. 8): $\nabla MR_e \approx \pm 0.013$ ml/mole and $\nabla E\sum_F - \sum_C \approx \pm 0.6\%$.

SUMMARY

1. It has been shown that alkyl β-aminovinyl ketones exist as a tautomeric mixture AlkCOCH = $CHNH_2 \rightleftharpoons$ ⇌AlkC (OH) =CH—CH =NH. Experimental proof of the existence of enamino-imido tautomerism has thus been given for the first time.

2. One tautomeric form (the α-form) of methyl β-aminovinyl ketone and of isobutyl β-aminovinyl ketone has been separated. On the basis of molecular refraction and infra-red spectra this form has been taken to have the most probable structure RC(OH)=CH–CH=NH.

3. The kinetics of the tautomeric change of the α-form of methyl β-aminovinyl ketone into the equilibrium mixture have been measured and the activation energy change for this change has been determined.

4. The influence of solvents on the position of tautomeric equilibrium in methyl β-aminovinyl ketone has been studied by the refractometric method; a slight shift towards the α-form has been observed in pyridine and dioxane.

5. The influence of temperature on the positon of tautomeric equilibrium in methyl β-aminovinyl ketone has been studied using the refractometric method; a slight shift towards the α-form has been observed when the temperature is increased.

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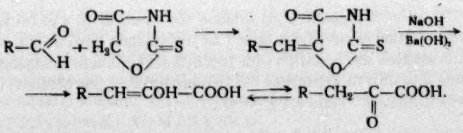
THE PREPARATION OF FURYL- AND ARYLPYRUVIC ACIDS BY HYDROLYSIS OF 5-ARYLIDENE-2-THIO-OXAZOLIDONES-4

T. E. Gorizdra and S. N. Baranov

Substituted phenylpyruvic acids find application in the preparation of α-aminoacids, pteridines and other materials. The existing methods of preparing these acids, such as, for example, the alkaline hydrolysis of arylidene derivatives of five-membered heterocyclic compounds [1], the acid hydrolysis of piperdine derivatives of α-β unsaturated esters [2], the condensation of oxalates with nitriles of phenylacetic acid [3] or with aromatic compounds containing a methyl or nitro group [4] often requires materials which are not readily available or do not make it possible to prepare acids with different substituents in the benzene ring. The aim of our research was to work out a method for preparing substituted phenylpyruvic acids in which cheaper and more readily available starting materials could be used and which would make it possible to introduce different substituents into the phenyl radical. It is known from the literature that phenylpyruvic acid is formed by the alkaline hydrolysis of 5-benzylidene-2-thio-oxazolidone-4 [5]. This property of 5-arylidene-substituted 2-thio-oxazolidones-4 formed the basis for the method of preparing substituted phenylpyruvic acids presented below.

The 2-thio-oxazolidone-4 required for the synthesis of the arylidene derivatives was prepared by a method described by one of us [5] from formaldehyde and the salts of cyanic and thiocyanic acids in hydrochloric acid. The various 5-arylidene derivatives were prepared by the condensation of 2-thio-oxazolidone-4 with different aromatic aldehydes, and also with furfural in acetic acid in the presence of sodium acetate [5]. The 5-arylidene-2-thio-oxazolidones-4 obtained in this way were subjected to alkaline hydrolysis by solutions of sodium or barium hydroxides, and the substituted phenylpyruvic acids, which are sparingly soluble in water, were separated by acidifying the hydrolyzates:



The experimental results are given in the table.

EXPERIMENTAL

Phenylpyruvic acid. 400 ml of 10% barium hydroxide solution was added to 10 g of 5-benzylidene-2-thio-oxazolidone-4 and the mixture boiled for 20 minutes. It was then cooled and acidified with 10% hydrochloric acid. A white precipitate of phenylpyruvic acid separated. M.p. after recrystallization from chloroform 156-157°. Yield 6.67 g (83%).

R	Melting point of the 5-arylidene-2-thio-oxazolidone-4	arylpyruvic acids	
		exptl. data	literature data
C_6H_5—	188°	156—157°	157°
o-ClC_6H_4—	170—171 *	150—151	152
C_6H_5CH=CH—	176	187—190	189—193
m-$NO_2C_6H_4$—	213	180 *	— — —
o OHC_6H_4—	202	151 **	152—153
C_4H_3O—	231 *	129—130	131
p-$(CH_3)_2NC_6H_4$—	223	>285	— — —
p-(OH)-m-(OCH_3)-C_6H_3—	237—238 *	159—160	161

* Product prepared for the first time.

** Isolated as the lactone.

o-Chlorophenylpyruvic acid. For the preparation of 5-o-chlorobenzylidene-2-thio-oxazolidone-4, 5.85 g (.05 mole) of o-chlorobenzaldehyde, 5 g of anhydrous sodium acetate and 25 ml of glacial acetic acid were placed in a flask fitted with reflux condenser. The mixture was heated to boiling over a period of 1 hour. It was then cooled, 100 ml of water was added and the pale yellow crystals of 5-o-chlorobenzylidene-2-thio-oxazolidone-4 filtered off. The product was readily soluble in alcohol, ether, acetone, chloroform and isoamyl alcohol; soluble in benzene and m-xylene only on heating; insoluble in water. After recrystallization from aqueous alcohol it formed pale yellow leaflets with m.p. 170-171°. Yield 8.8 g (73%).

Found %: N 6.06. $C_{10}H_6O_2NSCl$. Calculated %: N 5.84.

5 g 5-o-chlorobenzylidene-2-thio-oxazolidone-4 was heated to boiling over a period of 30 minutes with 50 ml of 10% caustic soda. After cooling, the solution was acidified with hydrochloric acid and the o-chlorophenylpyruvic acid filtered off. After crystallization from aqueous alcohol the acid melted at 150—151°. Yield 2.9 g (68%).

β-Styrylpyruvic acid. 250 ml of 20% caustic soda solution was added to 10 g of 5-cyanamylidene-2-thio-oxazolidone-4. The red-brown solution obtained was boiled for 3-4 minutes until a faint turbidity appeared. After cooling and filtration the solution was acidified with 10% hydrochloric acid to separate the β-styrylpyruvic acid, which is sparingly soluble in water. A crystalline sand-colored powder was obtained by crystallization from m-xylene, m.p. 187-190° (with decomp.). Yield 6.1 g (75%).

m-Nitrophenylpyruvic acid. 11.7 g (0.1 mole) 2-thio-oxazolidone-4, 15.1 g (0.1 mole) m-nitrobenzaldehyde, 10 g anhydrous sodium acetate and 50 ml glacial acetic acid were placed in a flask fitted with reflux condenser. The mixture was boiled on a wire gauze for 1½ hours. When the mixture had cooled, 100 ml of water were added; a precipitate of 5-m-nitrobenzylidene-2-thio-oxazolidone-4 separated, which was purified by crystallization from aqueous acetic acid. M.p. 213°. Light sand-colored crystals, readily soluble in alcohol, acetone, acetic acid; soluble with difficulty in chloroform, benzene, m-xylene, ether and dioxane; insoluble in water. Yield 19.4 g (77%).

Found %: N 11.32. $C_{10}H_6O_4N_2S$. Calculated %: N 11.20.

10 g of 5-m-nitrobenzylidene-2-thio-oxazolidone-4 was heated to boiling with 250 ml of 5% caustic soda

solution. The solution was cooled, filtered and acidified with hydrochloric acid. The precipitate of m-nitrophenylpyruvic acid which separated was purified by dissolving in acetic acid and reprecipitation with water. An aqueous solution of this acid forms an intense green coloration with $FeCl_3$. M. p. 180°. The product had a light brown color, readily soluble in alcohol, acetone, acetic acid, isoamyl alcohol and alkali solutions; soluble with difficulty in chloroform and dioxane; insoluble in water. Yield 5.7 g (68%).

Found %: N 6.81. $C_9H_7O_5N$. Calculated %: N 6.70.

The lactone of o-hydroxyphenylpyruvic acid. 150 ml of 10% barium hydroxide solution was added to 7.5 g of 5-salicylidene-2-thio-oxazolidone-4. The mixture was boiled for 2 hour in a flask fitted with reflux condenser. During this time the color of the solution changed from red-orange to yellow. The contents of the flask were cooled and acidified with hydrochloric acid and the lactone of o-hydroxyphenylpyruvic acid filtered off. The product was purified by crystallization from water. White needle-like crystals with m.p. 151°. Yield 4.8 g (78.5%).

Furylpyruvic acid. 11.7 g (0.1 mole) of 2-thio-oxazolidone-4, 9.6 g (0.1 mole) furfural, 10 g anhydrous sodium acetate and 50 ml glacial acetic acid were placed in a flask fitted with reflux condenser and boiled for 1 hour. The mixture was cooled, 250 ml of water added, and the greenish-brown crystals of 5-furfurylidene-2-thio-oxazolidone-4 which formed were separated by filtration and purified by crystallization from aqueous alcohol. M. p. 231°. The product was readily soluble in alcohol, acetone, dioxane and isoamyl alcohol; soluble on warming in benzene, m-xylene and chloroform; insoluble in water. Yield 13.6 g (70%).

Found %: N 7.22. $C_8H_5O_3NS$. Calculated %: N 7.18.

10 g of 5-furfurylidene-2-thio-oxazolidone-4 was ground in a mortar with 15 ml of 10% caustic soda. The black solution which formed was left at room temperature for 2 hours and then acidified with concentrated hydrochloric acid. The grey-green mass of furylpyruvic acid which separated was purified by crystallization from toluene. Fine light grey needles with m.p. 129–130°. Yield 2.8 g (35.5%).

p-Dimethylaminophenylpyruvic acid. 10 g of 5-p-dimethylaminobenzylidene-2-thio-oxazolidone-4 was boiled in a flask for 5 minutes with 400 ml of 5% caustic soda. During this time the initial red-orange color of the solution changed to yellow. The solution was cooled and acidified with 10% acetic acid. The brown precipitate which separated was purified by crystallization from aqueous alcohol. p-Dimethylaminophenylpyruvic acid was obtained as a brown fine crystalline powder which did not melt on heating to 285°. Readily soluble in alcohol, chloroform and solutions of mineral acids and of alkalies; soluble with difficulty in acetone, benzene, m-xylene, dioxane and isoamyl alcohol. An alcohol solution of p-dimethylaminophenylpyruvic acid does not give a coloration with $FeCl_3$ solution. Yield 2.5 g (30%).

Found %: N 6.83. $C_{11}H_{13}O_3N$. Calculated %: N 6.76.

4-Hydroxy-3-methoxyphenylpyruvic acid. 11.7 g (0.1 mole) 2-thio-oxazolidone-4, 15.2 g (0.1 mole) vanillin, 10 g anhydrous sodium acetate and 50 ml glacial acetic acid were boiled for 1 hour in a flask fitted with a reflux condenser. The mixture was cooled, 250 ml of water added and the 5-vanillinidene-2-thio-oxazolidone-4 filtered off and purified by crystallization from aqueous alcohol. Bright yellow needles with m.p. 237–238°. Readily soluble in alcohol and acetone; soluble on heating in acetic acid, dioxane, isoamyl alcohol, m-xylene and water; soluble with great difficulty in benzene and chloroform. Yield 9.2 g (66%).

Found %: N 5.76. $C_{11}H_9O_4NS$. Calculated %: N 5.58.

5 g of 5-vanillinidene-2-thio-oxazolidone-4 was dissolved in 100 ml of 20% caustic soda. The bright-red solution which formed was heated to boiling. The solution was then cooled, acidified with concentrated hydrochloric acid and extracted twice with 25 ml portions of ether. The ether was removed and the residue recrystallized from a small quantity of water. M.p. 159–160°.

SUMMARY

The following compounds, which are not described in the literature, have been synthesized and characterized: 5-o-chlorobenzylidene-, 5-m-nitrobenzylidene-, 5-furfurylidene- and 5-vanillinidene-2-thio-oxazolidone-4. The following α-ketoacids have been prepared by the alkaline hydrolysis of 5-furfurylidene- and 5-arylidene-2-thio-oxazolidones-4: phenyl-, o-chlorophenyl-, β-styryl-, furyl-, 3-methoxy-4-hydroxyphenyl-, m-nitrophenyl- and p-dimethylaminophenylpyruvic acids and the lactone of o-hydroxyphenylpyruvic acid with yields of from 30 to 80%. The method may be recommended for the preparation of furyl- and phenylpyruvic acids.

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THE EFFECT OF ACIDS AND ALKALIS ON ABSORPTION SPECTRA OF PYRIDINE DYES

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Salt-like dyes are salts of weak bases and strong acids, or, vice versa, of weak acids and strong bases, and can hydrolyze in aqueous solvents to a greater or lesser extent. The intensified color which is sometimes observed on dilution of alcoholic solutions of pyridine dyes, i.e., derivatives of primary aromatic amines, has been explained by us as being due to hydrolysis, and in order to suppress this hydrolysis when determining absorption curves we added hydrochloric acid to the alcoholic solutions of these dyes [1]. However, bearing in mind the structure of pyridine dyes, which in the case of derivatives of primary amines may be represented by the formula $[R-NH-(CH)_5=NHR]^+Cl^-$, it may be assumed that in the presence of a sufficient concentration of the acid not only is hydrolysis suppressed, but salt formation with the amino groups becomes possible. Schwarzenbach and Sulzberger [2] attribute the intensification of the color of pyridine dyes in the presence of acids (pH >5) to the formation of the bivalent ion $[RH_2N-(CH)_5=NHR]^{++}$.

In order to elucidate the behavior of pyridine dyes in neutral solutions and in the presence of acids, in relation to the valency of the cation, we have carried out a spectroscopic investigation of eleven dyes – derivatives of the following amines: aniline, p-toluidine, p-anisidine, p-aminophenol, p-aminodimethylaniline, ethyl ester of p-aminobenzoic acid, m-nitroaniline, p-nitroaniline, α- and β-naphthylamines.

In the presence of acids pyridine dye can undergo cyclization with the formation of chloroarylates of pyridine [3]. In the presence of acids and alkalis they can decompose, by hydrolysis, into glutaconic dialdehyde and amines, and for the purpose of comparison we have determined the spectra of glutaconic dialdehyde and its Na-enolate, of the chlorophenylate and p-nitrochlorophenylate of pyridine, and of p-nitroaniline.

The effect of acids on absorption spectra of dyes has been studied by many authors, and in particular, triarylmethane dyes [6, 7] and azodyes [4, 5] have been investigated in great detail. A. I. Kiprianov, L. S. Pupko and S. G. Friedman [8] have studied the effect of acids and alkalis on various groups of cyanine dyes; other studies in this field are also known.

The absorption spectra of the dyes studied in the present paper were determined in the visible region at 96° in alcohol containing various amounts of hydrochloric acid with an excess of carbonic acid, and in glacial acetic acid. In the case of aniline, p-anisidine, α- and β-naphthylamine and p-nitroaniline derivatives, the spectra were also determined in the ultraviolet, in the presence of alkali and hydrochloric acid. Absorption spectra of the aniline derivative were determined in concentrated sulfuric acid and in sulfuric acid diluted with alcohol.

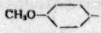
The stability of the alcoholic solutions was checked by determining the variation of the maximum optical densities with time (Table 1).

Evaluation of the absorption spectra. Figures 1 and 2 illustrate the absorption spectra of the aniline derivative. In neutral alcoholic solutions the curve has two maxima – at 405 and 485 mμ. On gradual addition of alkali the intensity of the shortwave band increases, reaches a maximum in the presence of 10 equivalents of sodium hydroxide and does not change on further addition of excess alkali; the intensity of the longwave band falls off gradually (Fig. 1). The action of the acid is analogous: the intensity of the longwave band increases while the shortwave band gradually disappears (Fig. 2). The nature of the changes in the spectra shows that in neutral alcoholic solutions the equilibrium: salt⇌base is attained; the acid shifts the equilibrium toward the salt side, the alkali-toward the base. Temperature plays an important part in this equilibrium: at 15-16° the

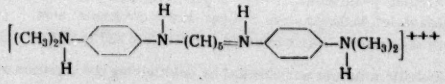
salt and the base are present in the solution in nearly equal amounts, with only a slight excess of the salt; at 25° the shortwave band of the curve is twice as high as the longwave band. On addition of a considerable excess of acid the intensity of the fundamental band in reduced and at the same time there appears a new band in the ultraviolet with a maximum at 265 mμ, which coincides with the absorption band of pyridine chlorophenylate; a large excess of acid (thousands of equivalents) facilitates partial cyclization of the dye [3]. The position of the maximum in the longwave region, which is independent of the amount and nature of the acid, remains the same. The absorption spectra of the aniline derivative in CH_3COOH, in alcohol containing excess carbonic acid and in alcohol containing hydrochloric acid coincide with each other. A similar behavior to that of the aniline derivative is shown by dyes containing electron donor substituents in the benzene ring, with only a difference in the degree of hydrolysis, as may be seen by comparing the data in Table 2 with the absorption spectra of the p-anisidine derivative (Figs. 3, 4). Somewhat different from the aniline derivative and from dyes which have an electron donor group in the benzene ring, is the p-aminodimethylaniline compound (Fig. 5). In the presence of a slight excess of acid (up to 100 equivalents) the intensity of the fundamental band increases somewhat, but the maximum of the band is not shifted; hydrolysis is suppressed. On addition of 1000 or more equivalents of hydrochloric acid the absorption maximum is gradually shifted to shorter waves; the maximum displacement amounts to 65 mμ.

TABLE 1

Variation of D_{max} of Alcoholic Solutions of Dyestuffs $[R-NH-(CH)_5=NHR]^+Cl^-$ with Time

R	Time (in minutes)				
	0	15	30	60	60 × 24
	0.8	0.8	0.8	0.8	0.6
	1.0	1.0	1.0	1.0	0.9
	1.05	1.05	1.05	1.05	0.95
	1.4	1.4	1.4	1.4	1.4
	1.1	0.9	0.6	0.5	0.05
	0.9	0.6	0.5	0.4	0.05

Intensfied color in this case is undoubtedly due to salt formation with the dimethylamino groups, and as the trivalent cation formed



easily undergoes hydrolysis, it can exist only in the presence of a large excess of acid. In the presence of a large excess of acid the absorption maximum of this dye coincides with that of the aniline derivative (485 mμ). By examining the absorptions of the naphthylamine derivatives it is possible to follow the effect of the condensed aromatic radical on the color and hydrolysis of pyridine dyes. As will be seen from a comparison of the spectra (Figs. 6 and 7) and the data in Table 2, isomeric naphthyl derivatives differ greatly among themselves as well as from the aniline derivative. The considerable intensification of color of the α-isomeride and its low resistance to hydrolysis are probably connected with a decrease of its basicity as a result of the appearance of

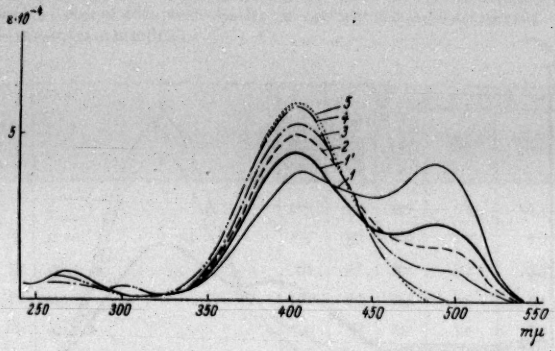


Fig. 1. Absorption curves of the aniline derivative in the presence of alkali (at 15°). 1) in 96% alcohol at 15°, 1') ditto, at 25°, 2) ditto + 1 equiv. NaOH, 3) ditto, + 2 equiv. NaOH, 4) ditto + 10 equiv. NaOH, 5) ditto + large excess of NaOH.

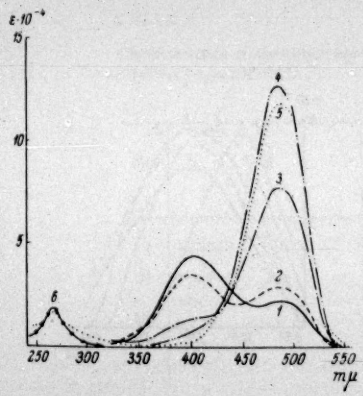
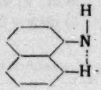


Fig. 2. Absorption curves of the aniline derivative in the presence of acid (at 25°). 1) in 96% alcohol, 2) ditto + 1 equiv. HCl, 3) ditto + 2 equivs. HCl, 4) ditto + 10 equivs. HCl, 5) ditto + large excess of HCl, 6) pyridine chlorophenylate in 96% alcohol.

steric hindrance effects  The hypsochromic shift of the α-isomerides is also observed in the case of some other naphthalene derivatives [9]. The data given in Table 2 show the variation of the extinction coefficients with the amount of hydrochloric acid in solutions of dyes with electron donor groups.

Comparing the dyes (I-V) we can observe a simple relationship: as the basicity of the cation increases the color of the dye deepens and its degree of hydrolysis decreases, as will be seen from a comparison of the differences between the extinction coefficients in acid and neutral solutions ($\varepsilon_2 - \varepsilon_1$). From the comparison of the spectra and data in Table 2 it will be seen that in the presence of excess acid the absorption maximum is either unchanged or is displaced to longer waves; consequently, in acid alcoholic solutions the proton does not combine with the cation even in the presence of strong electron donor groups. The low basicity of secondary amino groups of the dyes investigated is mainly due to the influence of the unsaturated pentamethinic chain. Depending on the nature of the radical attached to the nitrogen, the basicity of the cation may, likewise, vary. For example, substitution of hydrogen atoms on the nitrogen by methyl groups results in a decrease of the degree of hydrolysis of the dye, but when dyes which are derivatives of secondary amines are acted upon by acids no deepening of the color is observed. These problems require further investigation.

Table 3 contains data characterizing the behavior of dyes with electron acceptor groups in neutral and acid alcoholic solutions.

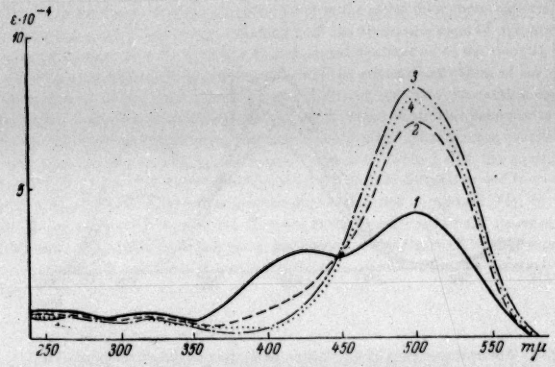


Fig. 3. Absorption curves of the p-anisidine derivative in the presence of acid. 1) in 96% alcohol, 2) ditto + 2 equivs. HCl, 3) ditto + 10 equivs. HCl, 4) ditto + large excess of HCl.

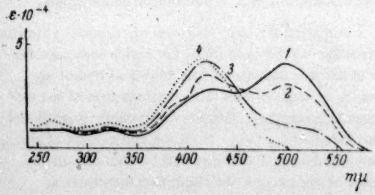


Fig. 4. Absorption curves of the p-anisidine derivative in the presence of alkali. 1) in 96% alcohol, 2) ditto + 2 equivs. NaOH, 3) ditto + 10 equivs. NaOH, 4) ditto + large excess of NaOH.

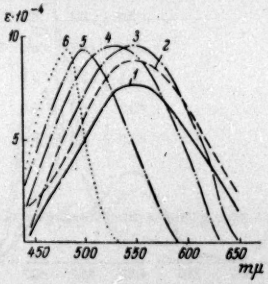


Fig. 5. Absorption curves of the p-aminodimethylaniline derivative in acid solutions. 1) in 96% alcohol, 2) ditto + 10 equivs. HCl, 3) ditto + 100 equivs. HCl, 4) ditto + 1000 equivs. HCl, 5) ditto + 3000 equivs. HCl, 6) ditto + 10,000 equivs. HCl.

The behavior of the ethyl p-aminobenzoate derivative differs little from similar derivatives containing electron donor substituents (cf. Table 2). The p-aminobenzoic acid derivative is hydrolyzed to a considerable extent and only in the presence of a large excess of hydrochloric acid is hydrolysis suppressed, giving a higher maximum. Nitro derivatives exist in the form of salts only in the presence of a large excess of acid. Figures 8 and 9 show the absorption spectra of the p-nitroaniline derivative. In neutral solution the curve has one absorption band with a maximum at 410 mμ. On acidifying the stock solution with excess acid a red color appears,

TABLE 2

Characteristics of Absorption Spectra of Solutions of Dyes of the Formula $[R-NH-(CH)_5=NHR]^+Cl^-$

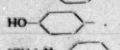
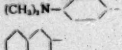
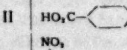
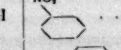
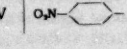
No.	R	λ max in ethyl alc. in mμ	$\epsilon_1 \cdot 10^{-4}$ in ethyl alc.	λ max in alc. w/excess HCl (mμ)	$\epsilon_2 \cdot 10^{-4}$ in alc. + HCl: 2 equiv. HCl	10 equiv. HCl	$\frac{\epsilon_2 - \epsilon_1}{10^2}$
I		485	4.2	485	7.7	12.7	8.5
II		495	5.3	495	7.7	9.9	4.6
III		500	4.1	500	8.7	8.2	4.1
IV		505	4.9	505	5.9	6.4	1.5
V		550	8.6	550	8.6	9.3	0.7
VI		422*	7.4	510	7.4	10.9	3.5
VII		410	5.3	480	—	7.0	7.0

TABLE 3

Characteristics of Absorption Spectra of Solutions of Dyes of the Formula $[RNH-(CH)_5=NHR]^+Cl^-$

No.	R	λ max in ethyl alc. in mμ	$\epsilon \cdot 10^{-4}$ in ethyl alc.	λ max in alc. w/excess HCl (mμ)	$\epsilon \cdot 10^{-4}$ in alc. + HCl: 2 equiv. HCl	10 equiv. HCl	large excess of HCl
I		505	4.7	505	7.3	7.3	7.3
II		500	4.2	500	4.2	4.2	6.3
III		—	—	500	—	—	6.8
IV		410	5.0	527	—	—	1.75

but on dilution with alcohol (to obtain the test solution) it disappears. The absorption spectrum of this solution shows three bands in the ultraviolet (Fig. 8, 2). As the acidified stock solution is gradually diluted (at first 5 times, then another five times) the red color remains unchanged and a broad band appears in the visible region with a maximum at 527 mμ. The nature of the change in the spectra in the presence of acid indicates that the solution contains an equilibrium mixture of different compounds. Concurrently with the formation of the dye salt there is formed, as a result of hydrolysis, the free base, and at the same time there takes place, in the presence of the acid, hydrolytic decomposition of the dye into glutaconic dialdehyde and p-nitroaniline. The band with the maximum at 305 mμ coincides with the absorption band of glutaconic dialdehyde (cf. Fig. 11). The bands situated in the middle ultraviolet probably belong to the equilibrium mixture: base ⇌ p-nitroaniline. On standing, or in the presence of large excess of acid, the acidified solution shows a band which almost coincides with the band given by p-nitroaniline in acidified alcohol; a band in the region of absorption by glutaconic dialdehyde

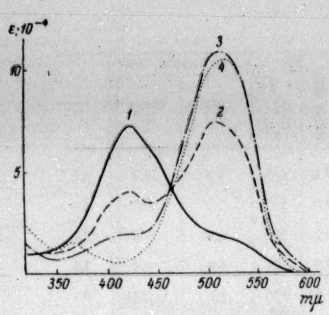


Fig. 6. Absorption curves of the α-naphthylamine derivative in the presence of acid. 1) in 96% alcohol, 2) ditto + 2 equivs. HCl, 3) ditto + 10 equivs. HCl, 4) ditto + large excess of HCl.

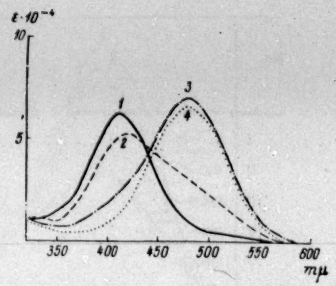


Fig. 7. Absorption curves of the β-naphthylamine derivative in the presence of acid. 1) in 96% alcohol, 2) ditto + 2 equivs. HCl, 3) ditto + 10 equivs. HCl, 4) ditto + large excess of HCl.

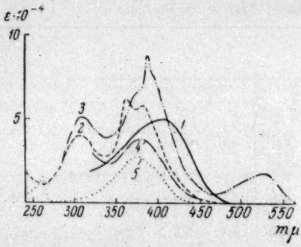


Fig. 8. Absorption curves of the p-nitroaniline derivatives in the presence of acid. 1) in 96% alcohol, 2) ditto + excess HCl, 3) ditto, on gradual dilution, 4) ditto + large excess of HCl, 5) p-nitroaniline in 96% alcohol + excess HCl.

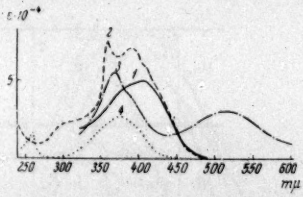
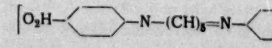


Fig. 9. Absorption curves of the p-nitroaniline derivatives in the presence of alkali. 1) in 96% alcohol, 2) ditto + 2 equivs. NaOH, 3) ditto + large excess NaOH, 4) p-nitroaniline in 96% alcohol.

is observed (not measured). A very similar situation is observed in the changes in the spectra of this dye in the presence of alkali (Fig. 9). In the presence of excess alkali the solution assumes at first a yellow coloration which rapidly changes to red, and a band appears in the longwave region with a maximum at 515 mμ which is due to the formation of the colored anion:



The band with the maximum at 367 mμ lies close to the band of the Na-enolate of glutaconic dialdehyde and to that of p-nitroaniline and probably belongs to a mixture of the two. It is known that spectra of mixtures sometimes occupy a mean position between those of the two components [10].

The behavior of pyridine dyes in concentrated sulfuric acid is interesting. Experiments have been carried out with the aniline derivative. The dye dissolves in the acid in the cold with the evolution of hydrogen chloride and almost complete decolorization. It could have been assumed that in concentrated sulfuric acid decomposition of the dye took place according to one or two possible mechanisms [1], but the spectrum of this solution does not show any bands belonging to the decomposition products (pyridine phenylate, aniline sulfate, or glutaconic dialdehyde). It is more probable that in the presence of sulfuric acid salt formation takes place

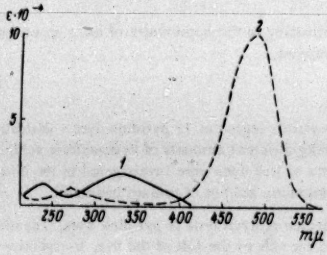


Fig. 10. Absorption curve of the aniline derivative. 1) in concentrated sulfuric acid, 2) in sulfuric acid solution diluted with alcohol.

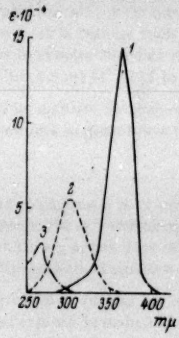


Fig. 11. Absorption curve of glutaconic dialdehyde. 1) Na-enolate of glutaconic dialdehyde in 96% alcohol, 2) glutaconic dialdehyde in 96% alcohol, 3) p-nitrochlorophenylate of pyridine in 96% alcohol.

with the secondary amino groups, although the proton can also add on to a carbon atom of the polymethinic chain $[R-NH-CH_2-CH-CH=CH-CH=NHR]^{++}$, and decolorization will take place owing to the disturbance of the conjugated system. The broad band in the near ultraviolet (Fig. 10) is possibly due to the formation of the bivalent cation. On dilution of the sulfuric acid solution with alcohol (0.7 ml to 25 ml) the intense orange coloration reappears; a band has been observed in the visible region with a maximum at 495 mμ and also a weak band in the region of absorption of pyridine phenylate. The shift of the absorption maximum of the fundamental band by 10 mμ to longer waves, as compared with its position in alcoholic solutions, is probably due to a change in the anion.

EXPERIMENTAL

Preparation and purification of the compounds. The dyes were prepared by the method of Zincke [11] and were purified by two recrystallizations from alcohol or by precipitation from alcohol with ether until all traces of dinitroaniline were removed (acetone solution tested with alkali). The p-nitroaniline derivative was obtained by the interaction of the Na-enolate of glutaconic dialdehyde with p-nitroaniline in the presence of hydrochloric acid.

1,5-Bis-(p-nitrophenylamino)-pentadien-1,3,5-chloride. The Na-enolate of glutaconic dialdehyde was obtained by the action of an excess of sodium hydroxide on pyridine sulfotrioxide [12]. It was recrystallized from methyl alcohol. Orange-yellow crystals.

Found %: Na 14.82, 14.66. $C_5H_5O_2Na \cdot 2H_2O$. Calculated %: Na 14.74.

A mixture of 0.6 g Na-enolate and 1.02 g of p-nitroaniline in 10 ml of ethyl alcohol was warmed on a water bath. On addition of a few drops of concentrated hydrochloric acid the solution boiled and assumed a red color. After 1-2 minutes when spontaneous boiling ceased, the mixture was brought to boiling on the water bath and kept at that temperature for a further 5-7 minutes and was then left to stand overnight. The precipitate was filtered off and washed with water, alcohol and ether. The yield of the crude product was 1.25 g; 0.5 g of the substance was dissolved in 250 ml of ethyl alcohol and after cooling the solution was acidified with a few drops of hydrochloric acid and left to crystallize. The next day the fluffy violet precipitate was filtered off. The dye contains alcohol of crystallization, m.p. 143-144°. Before analysis the substance was dried in vacuo at 65°.

Found %: N 15.02, 15.03. $C_{17}H_{15}N_4O_4Cl$. Calculated %: N 14.95.

The determinations of the absorption curves were carried out in the Goldberg spectrodensograph and in the spectrophotometer SF-4. The test solutions were prepared by the following method: A determined number of milliliters of the stock solution of the dye (2.5 mg in 50 ml of alcohol) was transferred to a measuring flask and diluted with an alcoholic solution of acid or alkali and the mixture was then diluted with alcohol to give a dye concentration of $1 \cdot 10^{-5}$ M (or $0.5 \cdot 10^{-5}$ M).

We wish to express our gratitude to V. N. Tolmachev for affording us the opportunity of using spectrophotometer SF-4 and for acquainting us with the operation of the instrument.

SUMMARY

1. The authors have investigated absorption spectra in the visible region of 11 pyridine dyes – derivatives of primary aromatic amines – in 96% alcohol, in alcohol containing different amounts of hydrochloric acid, with excess carbonic acid, and in glacial acetic acid. The spectra of five dyes were investigated in the ultraviolet in alcoholic solutions containing different amounts of hydrochloric acid or of sodium hydroxide.

2. The lower the basicity of the cations, the greater the degree of hydrolysis of pyridine dyes. The addition of acid to alcoholic solutions of the dyes shifts the equilibrium to the side of the salt of the dye, irrespective of the nature and amount of acid added.

3. Alkalis shift the equilibrium of alcoholic solutions of dyes with electron donor substituent groups to the base side. Alcoholic solutions containing excess alkali dyes with electron acceptor substituents are transformed into intensely colored anionoid dyes.

4. In concentrated sulfuric acid the aniline derivatives are decolorized as a result of salt formation. On further dilution of the sulfuric acid solution the original color of the dye is restored.

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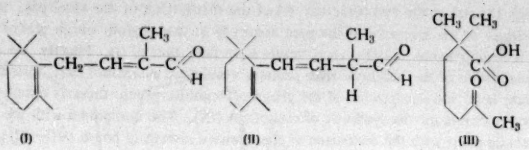
SYNTHETIC INVESTIGATIONS ON POLYENOID COMPOUNDS

XI. THE STRUCTURE OF 2-METHYL-4-(2',6',6',-TRIMETHYLCYCLOHEXEN-1'-YL)-BUTEN-2-AL-1

G. I. Samokhvalov, L. P. Zhukova, and N. A. Preobrazhensky

The interaction of β-ionone with esters of chloroacetic acid according to the Darzens reaction [1-3] has been investigated by many authors. The British investigators have pointed out the α, β-unsaturated character of the aldehyde formed in the reaction and have formulated its structure as 2-methyl-4-(2',6',6'-trimethylcyclohexen-1'-yl)-buten-2-al-1 (I). Milas and co-workers [4] when studying the decarboxylation under similar conditions, came to the conclusion that the main fraction of the aldehyde obtained has the structure of 2-methyl-4-(2',6',6'-trimethylcyclohexen-1'-yl)-buten-3-al-1 (II).

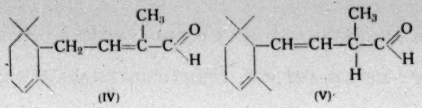


(I) (II) (III)

The main evidence in favor of structure (II) was the preparation of geronic acid (III) by ozonization of the aldehyde, this acid being usually formed on oxidation of compounds with the β-ionone structure, and the conservation of the power to absorb ultraviolet light in the region near 226 mμ irrespective of the transformations of the carboxyl group. These observations were accepted as proof that the absorption in the ultraviolet is the result of the conjugation of two carbon-carbon double bonds (as in II), and not of a carbon-carbon and a carbon-oxygen bond (as in I).

Attention has been drawn to the fact that in the condensation of samples of the pure aldehyde [5] with ethyl and hexenyl magnesium bromides and with sodium and lithium acetylides the carbinols obtained did not exhibit any marked absorption in the region of 226 mμ [6]. Ozonization of the pure aldehyde did not give geronic acid. In 1950 it was shown that ozonization of the substance with the structure (I) leads to the formation of small quantities of geronic acid, which vary with the conditions of experiment, and that this method may be used as a proof of the structure of the nucleus, but not of the position of the first double bond in the side chain [7]. 2,4-Dinitrophenylhydrazones and other derivatives possess light absorption properties which are characteristic of α,β-unsaturated aldehydes. Additional evidence for the structure (I) is provided by the existence in the Raman spectrum of the pure aldehyde of a band at 1630-1680 cm^{-1} which is characteristic of α, β-unsaturated carbonyl compounds [8]. Recently it has been shown [9] that the carbinol formed in the course of the regeneration of the aldehyde by the action of lithium aluminum hydride [10] can be oxidized by activated manganese dioxide in hexane solution, a property which is characteristic of allylic (α, β-unsaturated) alcohols. There is thus sufficient evidence in favor of structure (I) and the problem of the structure of this aldehyde could be regarded as definitely solved. However, Milas states [11] that "... chemical evidence collected in the author's laboratory over the last few years still favors strongly the structure (II)."

This difference of opinion regarding the structure of the product of condensation of β-ionone with esters of chloroacetic acid could possibly be attributed to the heterogeneous nature of the compound obtained. Evidence for this assumption may be found in the isolation of derivatives of the two isomeric aldehydes, (IV) and (V), from the corresponding products of condensation of the α,β-ionone, as described in 1952 [12].



(IV) (V)

In order to throw light on this problem we have investigated the substance formed from the condensation, saponification and decarboxylation, having subjected it to a careful fractionation. Figure 1 shows the graph of the refractive indices of the thirty fractions obtained. It will be seen that after separating the fractions containing unreacted β-ionone (Fractions 2-9), the distillation product was homogeneous. Analysis of the characteristic bands of infrared spectra of Fractions 2-9 shows that these fractions are a mixture of α-ionone with an increasing amount of the aldehyde (I). Figure 2 depicts the spectrum of infrared light transmitted by the aldehyde which has been purified through the crystalline semicarbazone (m.p. 155-156°). The position of the frequency ν CO 1680 cm^{-1} indicates conjugation of the carbonyl group with the unsaturated carbon-carbon bond. Figure 3 shows the sections of the corresponding spectra in the region 1800-1600 cm^{-1} for fractions separated at the beginning (Fraction 10) and at the end (Fraction 30) of the distillation of the aldehyde. Both groups of curves are an exact facsimile of the spectrum of the pure aldehyde in that region, which proves that the bulk of the reaction product is homogeneous and that its structure is, in fact, that of (I). Finally, we have found that in the course of the condensation of the aldehyde with primary vinylethynylcarbinol (VI), followed by selective hydrogenation of the triple bond and acetylation of the primary alcoholic group, there is obtained the compound (VII) which is the starting material for the synthesis of vitamin A (IX). The compound with the structure (VII) can undergo allylic rearrangement with the formation of the trienoid system of bonds (VII-VIII).

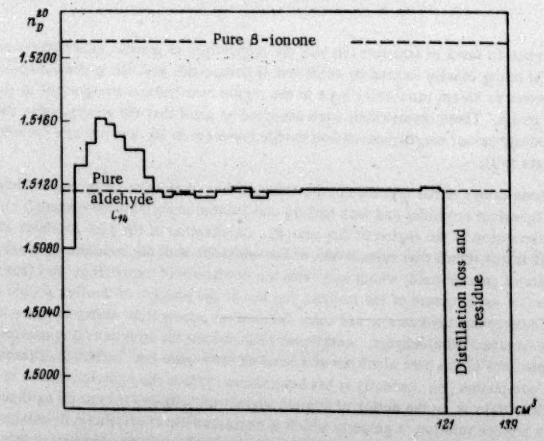
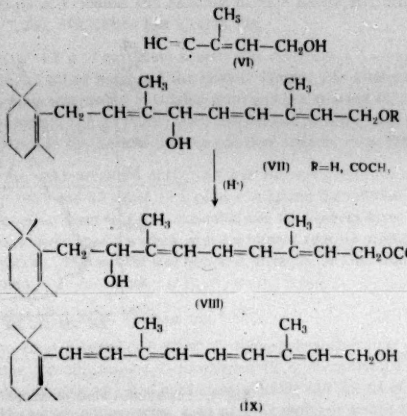


Fig. 1. Results of the fractionation of technical grade aldehyde. Refractive indices of the individual fractions.



(VI)

(VII) R=H, $COCH_3$

(VIII)

(IX)

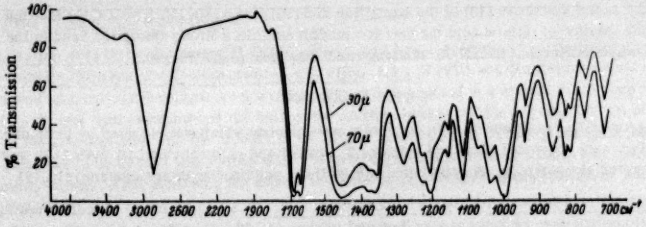
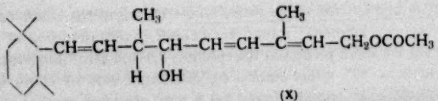


Fig. 2. Spectrum of infrared light transmitted by the aldehyde purified through its semicarbazone.

In the case of the corresponding derivative (X) of hypothetical aldehyde (II) allylic rearrangement with the formation of a trienoid conjugated system is not possible.



(X)

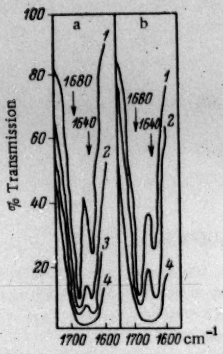


Fig. 3. Characteristic sections of the infrared transmission spectrum of fractions No. 10 (a) and No. 30 (b) of the aldehyde. 1) 10 μ, 2) 30 μ, 3) 70 μ, 4) 100 μ.

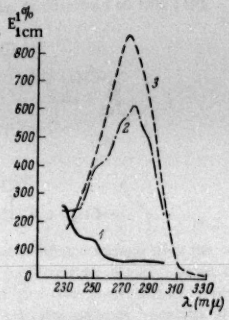


Fig. 4. Ultraviolet absorption spectra of the monoacetyl derivative of the diol (VII) and of its transformation products obtained by the action of dilute sulfuric acid. 1) original absorption; 2) absorption after 30 minutes; 3) absorption after three hours.

When the acetyl derivative [13] of the crystalline diol (VII) (m.p. 70-71°, R=$COCH_3$) is acted upon by dilute alcoholic solution of sulfuric acid the reaction product exhibits a strong absorption band in the region of 275-280 mμ, which proves that the allylic rearrangement does take place (Fig. 4).

EXPERIMENTAL

Starting materials. β-ionone was obtained from pseudoionone which was prepared by three different methods starting from: 1) natural citral and acetone; 2) linalool and chloroacetoacetic ester [14], and 3) disubstituted unsaturated alcohols (e.g., dimethylvinyl carbinol) and acetoacetic ester (diketene) [15,16].

Condensation of β-ionone with esters of chloroacetic acid. 72.5 g (1.35 mole) of sodium methylate was added in small portions over 1½ hours to a well-stirred mixture of 192 g (1 mole) β-ionone (b.p. 96° at 0.3 mm) and 134.5 g (1.24 mole) of the methyl ester of chloroacetic acid (b.p. 130°) at a temperature of -10°, -15°. The reaction mixture was stirred for 4 hours at -10° and a solution of 85 g of sodium hydroxide in 575 ml of aqueous (80%) methanol added. The temperature of this mixture was gradually raised to 2-5° and the reaction continued for another two hours. 720 ml of water was then added and the mixture stirred at 20° until the thick dark-orange mass, which formed at first, was completely dissolved. The solution was extracted with ether (3 times with 300 ml-portions), the extract washed with aqueous solutions of sodium chloride and dried with magnesium sulfate. The solvent was removed in a current of nitrogen and the residue distilled in vacuo. The mobile oily substance had a faint yellow color. Yield of the aldehyde, 156 g (75.7%).

B.p. 98-104° (0.2 mm), n_D^{20} 1.5130.

Fractionation of the aldehyde in a column of the rotary type. 139 ml of the aldehyde obtained in the foregoing preparation was separated on a laboratory rotary type column into 30 fractions of 3-5 ml each. Conditions of fractionation: pressure (in the main portion of the column) 0.1-0.5 mm, temperature in the flask 110-116°, temperature in the column 54-57°, reflux number 40, distillation rate 14-15 ml/hour, efficiency at the bottom of the column 120-150 ml/hour, pressure drop 0.7-1.8 mm, effective number of plates 15 (determined on a dibutyl phthalate - diethyl phthalate mixture).

The starting material was split on fractionation into the following portions: light distillate 3.9 ml (2.8% of original quantity), mixture of β-ionone and aldehyde (I) 25.4 ml (18.3%), aldehyde (I) 91.7 ml (66.0%), residue in flask 10.0 ml (7.2%), distillation loss 8 ml (5.7%).

Semicarbazone of (I). 4.2 g of potassium acetate was dissolved in 7 ml of methanol, mixed with 3.8 g of semicarbazide chloride in 7.7 ml of water and the mixture filtered into a solution of 7.2 g of (I) [6] in 25 ml of methanol. The reaction mass was heated to boiling point and left to stand for a day at a temperature of 0-5°. The separated yellowish crystals, 6.3 g (78.8%), were filtered and recrystallized twice from alcohol. The semicarbazone of (I) was obtained in the form of lustrous colorless crystals, m.p. 155-156°, $E^{1\%}_{1cm\ 288m\mu}$ = 1340.

Decomposition of the semicarbazone of (I). 3.3 g of the semicarbazone of (I) was mixed with 20 ml of petroleum ether (b.p. 80-100°) and 45 ml of 15% sulfuric acid and the mixture refluxed in a current of inert gas for five hours. The organic layer was then separated and the aqueous layer extracted with petroleum ether (10 ml portions). The ether extract was washed with a saturated aqueous solution of sodium bicarbonate and dried with magnesium sulfate. The solvent was removed in vacuo, and the residue (2.3 g) distilled. Yield of the aldehyde, 2.0 g (77.5%).

B.p. 98-99° (0.2 mm) n^{20}_D 1.5114, $E^{1\%}_{1cm\ 230}$ mμ = 956.

1-Acetoxy-3,7-dimethyl-6-hydroxy-9-(2',6',6'-trimethylcyclohexen-1'-yl)-nonatriene-2,4,7 (VII). 4.5 g (1.015 mole) of crystalline 1,6-dihydroxy-3,7-dimethyl-9-(2',6',6'-trimethylcyclohexen-1'-yl)-nonatriene-2,4,7(m.p. 70-71°) was dissolved in 14 ml of methylene chloride and 3.9 ml of pyridine. To the solution cooled to -5° there was gradually added, with stirring, 1.43 g (0.018 mole) of acetyl chloride in 5 ml of methylene chloride, and then the reaction mixture was stirred for one hour at -5° and left overnight at +25°. To bring about the decomposition, the reaction mixture was poured into ice water (10 ml), the organic layer was separated and the aqueous layer was extracted with methylene chloride (10 ml). The extract was washed with water, dried with magnesium sulfate and evaporated in vacuo. An oily light-yellow substance was obtained, yield 4.7 g (91.5%)

n^{20}_D 1.5060; $E^{1\%}_{1cm\ 230}$ mμ = 253 (Fig. 4).

Isomerization of (VII) by the action of dilute sulfuric acid into 1-acetoxy-3,7-dimethyl-8-hydroxy-9-(2',6',6'-trimethylcyclohexen-1'-yl)-nonatriene-2,4,6 (VIII). 4.5 g of (VII) was dissolved in 90 ml of ethanol; to this was added 22.5 ml of 5% sulfuric acid and the solution left to stand in a current of nitrogen for 30 minutes. A sample of 10 ml was then removed and the bulk of the mixture kept at 22° for 3 hours. 300 ml of water was then added to the reaction mass and the product of the allylic rearrangement extracted with petroleum ether (two 40 ml portions). The extract was washed with a saturated aqueous solution of sodium bicarbonate and dried with magnesium sulfate. After removing the solvent in vacuo an oily reddish-colored substance was obtained. Yield 3.6 g (80.0%)

n^{20}_D 1.5263, $E^{1\%}_{1cm\ 275}$ mμ = 870 (Fig. 4).

SUMMARY

1. Chemically pure 2-methyl-4-(2',6',6'-trimethylcyclohexen-1'-yl)-buten-2-al-1 was prepared by fractionating, in a rotary type column, the product of the condensation of beta-ionone with the methyl ester of chloroacetic acid (Darzens reaction).

2. By studying infrared transmission spectra of the individual fractions of the aldehyde it has been shown that the main product of the reaction is of homogeneous composition and that its structure is that of an alpha, beta-unsaturated carbonyl compound.

3. It was found that the product of condensation of beta-ionone with the methyl ester of chloroacetic acid (by the Darzens reaction) and the primary ethinylvinyl carbinol shows a tendency to undergo allylic rearrangement. This makes it possible to reach conclusions regarding the structure of the original aldehyde and to elucidate themechanism of dehydration in the synthesis of vitamin A.

4. The investigations described do not confirm the structure of 2-methyl-4-(2',6',6'-trimethylcyclohexen-1'-yl)-buten-3-al-1 proposed by Milas for the product of condensation of beta-ionone with esters of chloroacetic acid (by the Darzens reaction).

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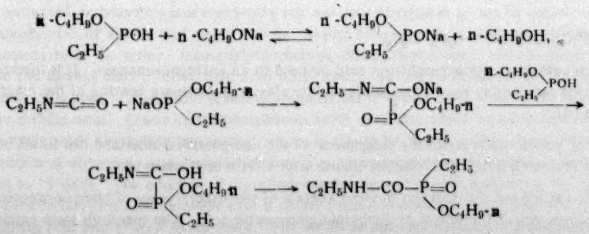
A NEW METHOD OF PREPARATION OF ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

XXVI. ADDITION OF INCOMPLETE ESTERS OF ACIDS OF PHOSPHORUS TO ETHYL ISOCYANATE, VINYLACETATE AND ESTERS OF UNSATURATED CARBOXYLIC ACIDS

A. N. Pudovik, I. V. Konovalova and R. E. Krivonosova

In continuation of our previous studies [1] we have investigated addition reactions of dialkylphosphorous and other acids to the ethyl ester of isocyanic acid, and we have extended our investigations on the addition of incomplete esters of various acids of phosphorus to vinyl acetate and to esters of unsaturated carboxylic acids containing different substituents attached to the carbon atoms linked by the double bond. Earlier [2] it had been shown that dialkyl-phosphorous and dialkyl-dithiophosphoric acids add on to the methyl ester of isocyanic acid.

In the absence of catalysts ethyl isocyanate reacts with dialkyl phosphorous, alkylphosphinous and dialkylthiophosphorous acids very slowly, and on mixing the reagents only a very slight rise of temperature takes place. The addition of the dry alcoholate accelerates the rate of reaction sharply; the temperature of the reaction mixture rises quickly to 80-100°. The reactions proceed more vigorously than with methyl isocyanate. In the case of the addition of the butyl ester of ethylphosphinous acid to ethyl isocyanate the reaction may be expressed by the following mechanism:



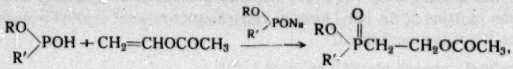
The products of reaction – esters of ethylamidophosphono- and of ethylamidothiophosphonoformic acid – are colorless liquids with an unpleasant odor, readily soluble in the usual solvents, and partly soluble in water (Table 1).

We have also attempted to bring about the addition of dialkylphosphorous acids to esters of isothiocyanic acids – phenyl and allyl isothiocyanates. There is no doubt that in the presence of sodium ethylate the reactions do take place, as may be gauged from the heating up of the reaction mixtures and from the considerable increase of viscosity as the reactions proceed. However, on distilling the reaction mixture in vacuo tarring takes place, accompanied by the evolution of white fumes and distillation of low-boiling products.

TABLE 1

Formula	Boiling point	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Phosphorus content (%) found	Phosphorus content (%) calc.	Yield (%)
$C_2H_5-NH-CO-P(=O)(OC_2H_5)_2$	167—168° (15mm)	1.4465	1.1294	49.40	49.00	14.64, 14.68	14.83	68
$C_2H_5-NH-CO-P(=S)(OC_2H_5)_2$	155—156 (12mm)	1.4811	1.1392	56.28	56.49	13.92, 14.10	13.77	39
$C_2H_5-NH-CO-P(=O)(OC_4H_9\text{-}n)(C_2H_5)$	177 (16mm)	1.4581	1.0589	57.07	56.60	13.63, 14.18	14.02	65

Earlier, one of us had shown that dialkylphosphorous acids easily add on to vinyl acetate [3]. In the present investigation we have succeeded in showing that vinyl acetate also adds on dialkylthiophosphorous acids and incomplete esters of alkyl- and arylphosphinous acids. The reactions were carried out according to the usual procedure. Sodium alcoholate was added to the reaction mixture, consisting of equimolar amounts of vinyl acetate and of the incomplete thiophosphorous or phosphinous esters, until it ceased to warm up. The reactions proceeded with a very short induction period. The temperature of the reaction mixture rapidly reached 80-90° and the mixture sometimes boiled. After warming for some time in the water bath the reaction mixtures were distilled in vacuo. The reactions proceed in accordance with the following mechanism:



where R=C_2H_5, n-C_4H_9, & R'=C_2H_5, C_6H_5.

where: R = C_2H_5, N-C_4H_9, and R' = C_2H_5, C_6H_5.

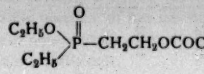
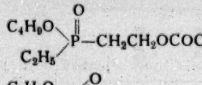
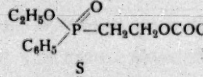
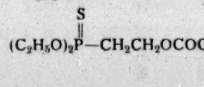
The reactions with diethylthiophosphorous acid proceed in an analogous manner. It is interesting to note that in the latter case satisfactory results are obtained only after a preliminary heating of the reaction mixture with triethylamine [4].

The constants, yields and analyses for phosphorus of the compounds synthesized are listed in Table 2. All the compounds described below are colorless liquids with a faint unpleasant odor.

We have also carried out the addition to vinyl acetate of the triethyl ester of phosphonacetic acid, of diethylphosphonacetone and of the nitrile of diethylphosphonacetic acid. The reactions were carried out in the presence of sodium ethylate, and were more vigorous than those with incomplete esters of acids of phosphorus. The temperature of the reaction mixtures rose to 50-60°. After heating on the water bath for two hours and neutralization of sodium ethylate with acetic acid the reaction mixtures were distilled in vacuo. A portion of the distillates of the starting materials, the residues, had the appearance of dark resinous masses which decomposed on further heating. On cooling, these residues solidified and cleared, and modifications of the experimental procedure did not give positive results. Attempts to isolate the reaction products by crystallization likewise did not give positive results.

Finally, we carried out the addition of incomplete esters of acids of phosphorus to esters of unsaturated mono- and dicarboxylic acids containing different substituents on the carbon atoms linked by the double bond.

TABLE 2

Formula	Boiling point	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Phosphorus content (%) found	Phosphorus content (%) calc.	Yield (%)
	110—111° (4 mm)	1.4361	1.0794	50.41	50.02	14.71, 14.62	14.62	48
	123 (4 mm)	1.4412	1.0408	59.88	59.26	12.50, 13.22	13.13	51.5
	149—150 (4 mm)	1.4990	1.1329	64.40	64.89	12.59, 12.62	12.11	35
	125—127 (16mm)	1.4590	1.1107	59.09	59.24	13.14, 12.99	12.99	33

As has already been observed earlier in the case of alpha, beta-unsaturated ketones and esters of monosubstituted homologues of acrylic acid [1], the presence of substituent groups on carbon atoms linked by a double bond retards the addition reactions. This is particularly evident when there is a phenyl group attached to the beta-carbon atom in esters of unsaturated carboxylic acids, and when there are two methyl groups in the beta-position in unsaturated ketones. The ease with which addition reactions take place also depends strongly on the volumes of the radicals contained in the reagents being added on. Dimethyl- and diethylphosphorous and thiophosphorous acids add on with the greatest ease; the dibutyl esters present some difficulty, and the phosphonacetic ester, phosphonacetone and the nitrile of phosphonacetic acid are still more difficult to add on. In order to bring about reactions with the latter compounds it is necessary to use larger amounts of the catalyst, to lengthen the induction period, and to heat the reaction mixture; under these conditions the yield of the addition products is lowered.

We have studied addition reactions of dialkylphosphorous and dialkylthiophosphorous acids to esters of alpha, beta-unsaturated carboxylic acids containing one and two substituent groups on the alpha- and beta-carbon atoms. The introduction of one methyl group into the diethyl ester of maleic acid had a comparatively small effect on the reactivity of the latter. Dimethylphosphorous, diethylphosphorous, and diisobutylthiophosphorous acids add on to the diethyl ester of citraconic acid fairly easily and the reactions proceed with a considerable evolution of heat. However, the addition products are obtained in lower yields than in the case of the analogous reactions of the maleic ester. Lower dialkylphosphorous acids were also added on to esters of alpha, beta-unsaturated carboxylic acids containing two methyl groups in the alpha, beta- or beta, beta-positions. The yields of addition products of dimethyl- and diethylphosphorous acids to ethyl esters of tiglinic and dimethylacrylic acids amounted to 13-44%. The addition of dimethylphosphorous and diethylphosphorous acids to the ethyl ester of beta, beta-dimethylacrylic acid proceeds with a longer induction period as compared with the reaction with the ester of tiglinic acid and gives a lower yield. The yields of addition products of analogous reactions which we have carried out previously with esters of acrylic and methacrylic acids, constitute 75-80%. The constants of the products obtained are given in Table 3.

We have not succeeded in bringing about the addition of dialkylphosphorous acids to the ethyl ester of β-methyl-β-phenylacrylic acid or of phosphonacetic acid to the diethyl ester of citraconic acid. Apparently, in these reactions steric hindrance effects play a decisive role. Such effects are due either to the larger volume of the substituent groups attached to the carbon atom of the unsaturated compound or due to the larger volume of the molecule being added.

All the reactions described in the present paper have been carried out by the procedure described by us in detail earlier [1].

TABLE 3

Formula	Boiling point	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Phosphorus content (%) found	Phosphorus content (%) calc.	Yield (%)
$(C_2H_5O)_2P(O)-C(CH_3)(COOC_2H_5)-CH_2COOC_2H_5$	182° (9 mm)	1.4385	1.1165	76.28	76.41	9.25, 9.75	9.56	64.50
$(C_2H_5O)_2P(S)-C(CH_3)(COOC_2H_5)-CH_2COOC_2H_5$	180—181 (9 mm)	1.4595	1.1205	83.18	83.90	9.40, 9.37	9.11	40.02
$(iso\text{-}C_4H_9O)_2P(S)-C(CH_3)(COOC_2H_5)-CH_2-COOC_2H_5$	196—197 (8 mm)	1.4620	1.0640	102.40	102.37	7.98	7.83	20.1
$(C_2H_5O)_2P(O)-CH(CH_3)-CH(CH_3)-COOC_2H_5$	142—143 (10 mm)	1.4330	1.0615	65.18	65.52	11.69	11.65	43.8
$(CH_3O)_2P(O)-C(CH_3)-CH_2-COOC_2H_5$	121—122 (10 mm)	1.4250	1.0821	56.10	56.28	13.15	13.02	21.05
$(C_2H_5O)_2P(O)-C(CH_3)-CH_2-COOC_2H_5$	131—132 (10 mm)	1.4310	1.0622	65.15	65.52	11.57	11.65	13.6

SUMMARY

1. It has been shown that the ethyl ester of isocyanic acid and vinyl acetate, in the presence of alkali metal alcoholates, easily add on dialkylphosphorous and dialkylthiophosphorous acids as well as the acid esters of alkyl phosphinous acids.

2. The authors have investigated addition reactions of incomplete esters of acids of phosphorus to ethyl esters of citraconic, beta,beta-dimethylacrylic and beta-methyl-beta-phenylacrylic acids. It has been indicated that the presence of two substituent groups on the alpha, beta- and particularly on the beta-carbon atoms in esters of unsaturated carboxylic acids gives rise to considerable steric hindrance which renders the addition reactions more difficult.

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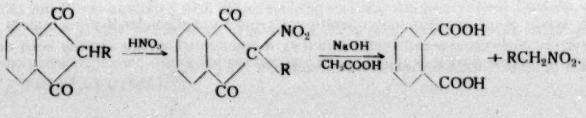
SYNTHESIS OF ω-NITROETHYL-p-NITROBENZENE

L. Zalukayev and E. Vanag

Some time ago one of us developed a method of preparation of primary nitro-compounds according to the equation:



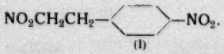
Using this method the following compounds have been prepared in satisfactory yields: phenylnitromethane [1], m-nitrophenylnitromethane [2], p-nitrophenylnitromethane [2], and alpha-quinolylnitromethane [3]. Later we synthesized alpha-naphthylnitromethane [4], 4-nitro-alpha-naphthylnitromethane [4], 4-bromo-alpha-naphthylnitromethane [5] and other compounds.

The main object of these studies was to investigate the value of this method as a preparative method, and this was done mainly by synthesizing arylnitromethanes and nitromethanes containing heterocyclic substituents, because the indandione-1,3 derivatives which are used as the starting materials, are easily accessible.

Because alkly derivatives of indandione-1,3 are less accessible and because there are less expensive and more practical ways of preparing nitroparaffins, we have limited ourselves to one investigation in which we have demonstrated the formation of nitropropane from 2-nitro-2-ethylindandione, a reaction which is of some theoretical interest [6].

The method developed for the preparation of arylnitromethanes and nitromethanes with heterocyclic substituents may also give good results in other cases.

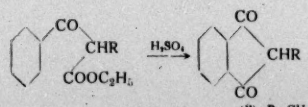
As an example we mention here the synthesis of ω-nitroethyl-p-nitrobenzene (I).



(I)

This compound is not listed in the literature. Only an unsuccessful attempt at its preparation has been described [7].

The starting material, 2-(p-nitrobenzyl)-indandione-1,3 (II), was obtained by Wojack's method [8], i.e., by cyclization of substituted benzoylacetic ester by the action of sulphuric acid:

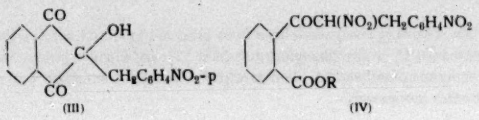


(II) R=CH$_2$C$_6$H$_4$NO$_2$(o)

The statement of this author that the diketone is obtained in a yield of about 70% could not be confirmed in our own experiments. First, we have found that p-nitrobenzylacetophenone is formed in considerable quantities, something which is not mentioned by Wojack. Second, the yield of the diketone amounted to 32% only. However, the problem requires some additional investigation which was not the object of our study.

Nitration of the diketone gave 2-nitro-2-(p-nitrobenzyl)-indandione-1,3 in 48% yield. The use of less concentrated acid lowers the yield of the nitro-derivative and leads to an intensification of oxidative processes which, in turn, leads to the formation of a new compound, i.e., 2-hydroxy-2-(p-nitrobenzyl)-indandione-1,3 (III).

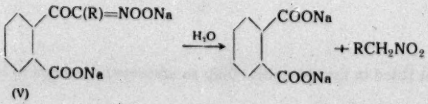
Under the action of sodium alcoholates 2-nitro-2-(p-nitrobenzyl)-indandione-1,3 gives esters of α-nitro-α-(p-nitrobenzyl)-acetophenone-o-carboxylic acid (IV), a reaction which has already been described by us in detail in the case of other 2-nitro-2-substituted indandiones-1,3 [2, 9].



(III) (IV)

The method of preparation of nitro-compounds which has been developed by us for the above mentioned nitromethanes with an aryl and a heterocyclic radical will be referred to as the "acetic acid method." This method consists of dissolving the nitrodiketone in alkali and acidifying the solution with dilute acetic acid, whereupon the arylnitromethane is precipitated and is easily separated. In the case of analogous compounds with an alkylaryl radical this method is unsatisfactory.

By synthesizing the two nitrodiketones: 2-nitro-2-benzhydryl-indandione-1,3 and 2-nitro-2-(p-nitrobenzyl)-indandione-1,3, we have developed the so-called "salt method". This method makes use of the previously described property of nitrodiketones to dissolve in alkalis with the formation of disodium salts of derivatives of alpha-nitro-acetophenone-o-carboxylic acid [1] (V). We have now found that when such derivatives contain an alkyl-aryl radical, their disodium salts easily decompose on heating their aqueous solutions, according to the equation:



(V)

Using this method we have succeeded in preparing o-nitroethyl-p-nitrobenzene in 70% yield and benzhydrylnitromethane in 50% yield based on the nitrodiketone. The structure of o-nitroethyl-p-nitrobenzene was proved by transforming it into nitrophenylacetic acid by the well-known reaction of primary nitro-compounds with sulfuric acid.

EXPERIMENTAL

1. Ethyl ester of p-nitrobenzylbenzoylacetic acid. To an alcoholic solution of sodium ethylate prepared from 12 g of the metal and 300 ml of anhydrous alcohol, there was added 100 g of benzoylacetic ester. The mixture was cooled by immersion in cold water and stirred mechanically for 40 minutes. During this period 113 g of p-nitrobenzyl bromide was added to the reaction mixture in small portions, disregarding the formation of a fine crystalline precipitate. At the end of this period the mixture was stirred for another 1½ hours, diluted with water to approximately 3 liters, the precipitate separated, washed with water, air-dried and recrystallized from 1,000 ml of ethanol. The substance was obtained in the form of yellowish-grey needles, m.p. 91-92°. Yield 145 g (85%).

2. 2-(p-Nitrobenzyl)-indandione-1,3. To 120 ml of concentrated sulfuric acid pre-heated to 105-110° was added 20 g of finely ground p-nitrobenzylbenzoylacetic ester with vigorous stirring. The ester dissolved rapidly with foaming, and the mixture assumed a dark-violet color. Immediately after dissolving the ester the mixture was rapidly cooled and poured into cold water. The precipitate, consisting of a mixture of p-nitrobenzylacetophenone and 2-(p-nitrobenzyl)-indandione-1,3, was separated into the components by adding 50 ml of a 10% sodium hydroxide solution to the reaction mixture and shaking vigorously. The deep red solution was filtered off from the undissolved substance, the residue was washed on the filter and the aqueous washings were combined with the filtrate. The latter was acidified with dilute sulfuric acid and the precipitated diketone was dried and recrystallized from 40 ml of glacial acetic acid. Yield 5.5 g (32%) large yellow crystals, m.p. 141-142°.

The p-nitrobenzylacetophenone which did not dissolve in the alkali, was recrystallized from alcohol and had m.p. 99-100°. Yield 8.35 g (54%).

Found %: C 70.42; H 5.00; N 5.66. M 227. $C_{15}H_{13}O_3N$. Calculated %: C 70.60; H 5.10; N 5.49. M 255.

The phenylhydrazone was prepared by heating 1 g of the ketone with 1 ml of phenylhydrazine in 10 ml of alcohol. Bright yellow crystals, m.p. 154-155°, were obtained from glacial acetic acid.

Found %: N 12.31. $C_{21}H_{19}O_2N_3$. Calculated %: N 12.17.

By refluxing with hydrochloric acid (1:1) the substance was saponified into the original product, m.p. 101°, which did not depress the melting point when mixed with a known sample.

3. Nitration of the diketone. (a) 11 g of 2-(p-nitrobenzyl)-indandione-1,3 was dissolved in 120 ml of glacial acetic acid. On cooling there was added 20 ml of nitric acid (d 1.52), the solution was shaken and cooled under the tap and was then diluted with water. The white precipitate was filtered off and recrystallized from alcohol, m.p. 158°. Recrystallization from acetic acid gave 6.2 g (48%) of yellow lustrous needles melting at 163-164°.

Found %: C 59.07; H 3.20; N 8.60. $C_{16}H_{10}O_6N_2$. Calculated %: C 58.89; H 3.07; N 8.59.

(b) 11 g of 2-(p-nitrobenzyl)-indandione-1,3 was dissolved by warming in 50 ml of glacial acetic acid. To the solution warmed to 70° there was added 20 ml of nitric acid (d 1.35). The yellow solution became colorless and evolved oxides of nitrogen. On cooling under the tap the nitro-derivative was precipitated in the form of yellow crystals, m.p. 160°. Yield 4.5 g (35%).

A second crop of crystals, 3.5 g, melting at 167° (III) was separated from the mother liquor after standing for a short time. Recrystallization from alcohol did not alter the melting point. The substance represents the oxidation product of the diketone (II).

Found %: C 64.77; H 3.50; N 4.98. M 332. $C_{16}H_{11}O_5N$. Calculated %: C 64.63; H 3.70; N 4.71. M 297.

By the action of acetyl chloride on the substance there was obtained the acetyl derivative in the form of colorless needles, m.p. 187°.

Found %: N 4.20. $C_{18}H_{13}O_6N$. Calculated %: N 4.10.

On heating the substance (m.p. 187°) in alcohol in the presence of a small amount of sulfuric acid, the characteristic odor of ethyl acetate was perceived. This confirms the presence of an acetyl group in the compound.

4. The action of sodium alcoholates on 2-nitro-2-(p-nitrobenzyl)-indandione-1,3. (a) The methyl ester of α-nitro-α-(p-nitrobenzyl)-acetophenone-o-carboxylic acid was obtained by the action of 3% sodium methylate in methanol on the nitrodiketone. Bright yellow elongated flakes, m.p. 112-113°, were obtained after recrystallization from alcohol. The yield was almost quantitative.

Found %: C 56.80; H 4.11; N 7.96. $C_{17}H_{14}O_7N_2$. Calculated %: C 56.96; H 3.91; N 7.82.

(b) The ethyl ester was obtained by a similar method by the action of sodium ethylate in anhydrous ethanol on 2-nitro-2-(p-nitrobenzyl)-indandione-1,3. Yellow crystals, m.p. 90-91°.

Found %: C 58.09; H 4.30; N 7.75. $C_{18}H_{16}O_7N_2$. Calculated %: C 58.08; H 4.30; N 7.53.

5. Preparation of nitro-compounds by the "salt" method. (a) 10 g of 2-nitro-2-benzhydrylindandione-1,3 was dissolved in 100 ml of 10% sodium hydroxide at 60° with mechanical stirring. When the substance was almost dissolved, the solution was filtered and left to crystalize. The crystals of the disodium salt weighed 7.5 g (64%).

7.5 g of the salt was dissolved in 100 ml of water and heated to boiling. The solution rapidly turned milk-white. On cooling the emulsion changed into a white powder, m.p. 69-70°, weighing 3.2 g (50%, based on the nitrodiketone). A mixture with an authentic sample did not depress the melting point.

(b) 10 g of 2-nitro-2-(p-nitrobenzyl)-indandione-1,3 was poured into 100 ml of sodium ethylate solution prepared from 100 ml of 96% alcohol and 3 g of the metal. When the substance dissolved there was added 30 ml of water and the mixture was left to stand at room temperature for 2 hours. The precipitate of the salt was filtered off and dissolved in water. The solution was heated to boiling, cooled and diluted with cold water. The yellow powdery nitro-derivative was filtered off and dried. Yield 3.8 g (70%), m.p. 98-99°. The substance crystallizes very well from alcohol in the form of large bright-brown needles. It is sparingly soluble in water but cannot be steam-distilled.

Found %: C 49.09; H 4.00; N 14.22. $C_8H_8O_4N_2$. Calculated %: C 48.98; H 4.08; N 14.29.

1 g of ω-nitroethyl-p-nitrobenzene was heated with 10 ml of 83.5% sulfuric acid for 15 minutes in such a manner as to continually produce a small amount of white fumes. After cooling, the reaction mixture was mixed with 10 ml of water. The precipitate was filtered off and treated with cold sodium carbonate solution. The unreacted nitro-compound remained in the residue, while the p-nitrophenylacetic acid went into solution. The bicarbonate extract was acidified and the white precipitate of p-nitrophenylacetic acid was separated and dried. M.p. 150-151°.

Found %: N 7.67. $C_8H_7O_4N$. Calculated %: N 7.74.

The mixture with an authentic sample [10] of p-nitrophenylacetic acid melts without depression at 150-151°.

SUMMARY

The authors have developed a method of preparation of ω-nitroethyl-p-nitrobenzene from 2-nitro-2-(p-nitrobenzyl)-indandione-1,3.

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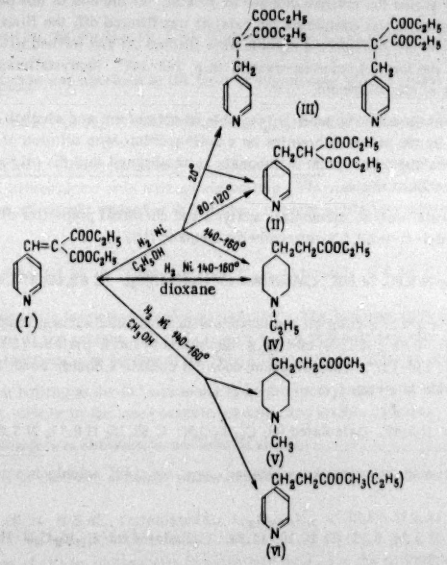
* T.p. = C. B. Translation pagination.

HYDROGENATION OF 4-(β,β-DICARBETHOXYVINYL)-PYRIDINE IN THE PRESENCE OF RANEY NICKEL CATALYST

E. S. Nikitskaya and M. V. Rubtsov

Hydrogenation of 4-(β,β-dicarbethoxyvinyl)-pyridine (I) in anhydrous ethyl alcohol in the presence of platinum black leads, as is well known, to the formation of 4-(β,β-dicarbethoxyethyl)-piperidine [1].

We have attempted to prepare this compound using Raney nickel as the catalyst. We have found that in this case, parallel with the hydrogenation, other reactions take place in various directions depending on the temperature conditions of the experiment.



Hydrogenation at room temperature leads to the formation of two compounds. One of these, obtained in 63.5% yield, is 4-(β,β-dicarbethoxyethyl)-pyridine (II), as has been confirmed by transforming it into β-(pyridyl-4)-propionic acid. The second compound, obtained in 13.9% yield, is found from molecular weight and analytical data to have the composition $C_{26}H_{32}O_8N_2$. Since this compound does not form either a sodium derivative or a bromo-derivative it probably corresponds to the formula (III).

If the hydrogenation is carried out at temperatures between 80-120° the reaction proceeds in one direction leading to the formation of compound (II) only.

The hydrogenation of the pyridine nucleus to the piperidine ring takes place at higher temperatures (140-160°). In the course of the reaction, decarbethoxylation to the monocarboxylic ester stage takes place with the simultaneous ethylation of the nitrogen giving the ethyl ester of β-(N-ethylpiperidyl-4)-propionic acid (IV) in 91% yield. A similar reaction takes place in methyl alcohol as the medium, in which case, in addition to decarboxylation and alkylation of the nitrogen, transesterification takes place with the formation of the methyl ester of β-(N-methylpiperidyl-4)-propionic acid (V). However, the reaction does not proceed to completion because a fraction separates from the reaction mass which appears to consist of a mixture of ethyl and methyl esters of β-(pyridyl-4)-propionic acid (VI); saponification of this fraction gives the free acid.

It is of interest to note that hydrogenation at 140-160° in dioxane as the medium likewise leads to the formation of (IV) in 52% yield. In this case the ethylation reaction obviously proceeds at the expense of the decarboxylation of the compound.

EXPERIMENTAL

Hydrogenation of 4-(β,β-Dicarbethoxyvinyl)-pyridine (I) in Ethyl Alcohol at Room Temperature

10 g of (I), 200 ml of anhydrous ethyl alcohol and 4 g of Raney nickel catalyst (in paste form), obtained by the usual method and washed with alcohol, was transferred into an autoclave (0.5 liter capacity). Hydrogen gas was charged into the autoclave to a pressure of 50 atm and the reaction mixture was stirred at room temperature for 8 hours, during which period the pressure dropped to 46 atm. At the end of this period absorption of hydrogen ceased. When the reaction was completed the catalyst was filtered off, the filtrate was evaporated in vacuo to a volume of 50 ml, and the precipitated crystals were filtered off and washed with a small quantity of ether. Yield 1.39 g (13.9%) in the form of colorless crystals, m.p. 145-147°. Recrystallization from alcohol did not change the melting point of the compound.

The compound does not contain a double bond, it is soluble in chloroform and alcohol, sparingly soluble in ether and insoluble in water. By the action of bromine on a boiling chloroform solution of the substance a perbromide is formed which on shaking with sodium bicarbonate is transformed into the original compound; it does not react with powdered metallic sodium.

A comparison of the molecular weight, elementary analysis and chemical properties of the substance supports the formula of 1,4-di-(pyridyl-4')-2,2,3,3-tetracarbethoxybutane (III).

Found %: C 62.59; H 6.73; N 5.85. M 508. Calculated for $C_{28}H_{32}O_8N_2$: C 62.40; H 6.40; N 5.60; M 500.

The mother liquor, obtained after filtering off the crystals with m.p. 145-147° was evaporated in vacuo and the residue distilled at 5 mm. 6.35 g (63.5%) of 4-(β,β-dicarbethoxyethyl)-pyridine (II) was obtained as an oily colorless liquid boiling at 156-157°. The compound does not contain a double bond, is soluble in the usual organic solvents and insoluble in water.

Found %: C 62.12; H 6.94 N 5.49. Calculated for: $C_{13}H_{17}O_4N$: C 62.15; H 6.77; N 5.57.

The hydrochloride of (II) is a white crystalline substance, m.p. 146-148°, soluble in water and hot alcohol, and insoluble in ether.

Found %: C 54.35, 54.20; H 6.34, 6.31; Cl 12.10, 11.88. Calculated for $C_{13}H_{17}O_4N \cdot HCl$: C 54.29; H 6.26; Cl 12.34.

Saponification of (II) followed by decarboxylation give β-(pyridyl-4)-propionic acid, m.p. 230-232°.*

1,4-Di-(pyridyl-4')-2,3-dicarboxybutane. 1 g of (III) in 10 ml of concentrated hydrochloric acid was heated for 8 hours with gentle boiling. The precipitate gradually dissolved, but was reprecipitated later. It was filtered off and washed with a small amount of alcohol and ether. A white substance was obtained (0.6 g)

* M. V. Rubtsov gives an m.p. of 232°[2].

which did not melt on heating up to 360°. The substance was dissolved in 2 ml of 15% sodium bicarbonate solution, the latter was filtered and precipitated with excess acetic acid. Yield 0.45 g (75%), m.p. 344-345°. The substance is insoluble in the usual organic solvents or in water.

Found %: N 9.26, 9.18. Calculated for $C_{16}H_{16}O_4N_2$: N 9.33.

Hydrogenation of (I) in ethyl alcohol at 80-120°. The hydrogenation was carried out as described above, but at a temperature of 80-120°. 10 g of (I) gave 7.07 g (70%) of compound (II), b.p. 156-157°, and approximately 2.5 g of a tarry residue.

Hydrogenation of 4-(β,β-Dicarbethoxyvinyl)-pyridine (I) in Ethyl Alcohol at 140-160°

Ethyl ester of β-(N-ethylpiperidyl-4)-propionic acid (IV). The hydrogenation was carried out as described above, but at a temperature of 140-160°. The process was complete within 30 hours. In the course of the hydrogenation of 10 g of the ester the pressure dropped from 50 to 16 atm, which corresponds to the amount of hydrogen required for the hydrogenation of the pyridine nucleus and of the double bond in the side chain. 7.55 g (91%) of a colorless oily substance, b.p. 107-110° (2 mm), was obtained. The substance does not react with benzoyl chloride, it is easily soluble in the usual organic solvents and soluble in water. Its aqueous solutions give an alkaline reaction to phenolphthalein.

Found %: C 67.61, 67.72; H 10.52, 10.89. Calculated for $C_{12}H_{23}O_2N$: C 67.60; H 10.79.

The picrate of (IV) had the form of bright yellow crystals, m.p. 162-164° (from alcohol).

Found %: C 48.70, 48.90; H 6.19, 5.90. Calculated for $C_{18}H_{26}O_9N_4$: C 48.86; H 5.88.

The hydrochloride was obtained in the form of hygroscopic white crystals melting at 104-106°.

Found %: Cl 14.20, 14.52. Calculated for $C_{12}H_{23}O_2N \cdot HCl$: Cl 14.22.

Hydrochloride of β-(N-ethylpiperidyl-4)-propionic acid. 1.92 g of (IV) was heated for 8 hours with 20 ml of concentrated hydrochloric acid with gentle boiling. The solution obtained was evaporated on the water bath to a thick mass which was treated with acetone. A white crystalline substance was obtained (1.6 g, 80.4%) m.p. 157-159°.

Found %: N 6.14; Cl 16.10. Calculated for $C_{10}H_{19}O_2N \cdot HCl$: N 6.32; Cl 16.02.

Hydrogenation of (I) in methyl alcohol at 140-160°. The hydrogenation is carried out as described above using methyl alcohol as the solvent. 10 g of (I) gave 4.05 g of a colorless oily substance which on distillation at 1 mm gave two fractions, one boiling at 94-96° (1.75 g), and the other at 104-106° (1.87 g).

The substance boiling at 94-96° was found to be the methyl ester of β-(N-methylpiperidyl-4)-propionic acid (V). It is very soluble in the usual organic solvents, and soluble in water.

The hydrochloride was obtained in the form of an oil.

The picrate is in the form of bright yellow crystals, m.p. 195-197° (from alcohol).

Found %: C 46.34 H 5.45. Calculated for $C_{16}H_{22}O_9N_4$: C 46.37; H 5.31.

Saponification of (V) by boiling with hydrochloric acid gave the hydrochloride of β-(N-methylpiperidyl-4)-propionic acid in the form of white crystals, m.p. 168-170°, which are very soluble in water and soluble in alcohol.

Found %: N 7.01, 7.15; Cl 17.38, 17.58. Calculated for $C_9H_{17}O_2N \cdot HCl$: N 6.74; Cl 17.10.

The fraction boiling at 104-106° (1 mm) apparently consists of a mixture of the ethyl and methyl esters of β-(pyridyl-4)-propionic acid and on saponification with hydrochloric acid gave the hydrochloride of β-(pyridyl-4)-propionic acid, m.p. 110-112°.*

Found %: N 7.53, 7.80; Cl 18.60, 18.73. Calculated for $C_8H_9O_2N \cdot HCl$: N 7.46; Cl 18.93.

Hydrogenation of (I) in dioxane at 140-160°. Hydrogenation was carried out as above, using dioxane as the solvent. 10 g of (I) gave 4.5 g (52.6%) of a colorless oil boiling at 108-110° (2 mm). 3.5 g of a tarry residue remained in the distillation flask.

The picrate is in the form of yellow crystals, m.p. 162-163°. The melting point of a mixture of the substance with the picrate of the ethyl ester of β-(N-ethylpiperidyl-4)-propionic acid was not depressed.

Found %: C 48.95, 48.74; H 5.81, 5.84. Calculated for: $C_{19}H_{22}O_9N_4$: C 48.86; H 5.88.

SUMMARY

Hydrogenation of 4-(β,β-dicarbethoxyvinyl)-pyridine in anhydrous alcohol in the presence of Raney nickel catalyst leads to the formation of different compounds, depending on the conditions of the reaction. When the reaction is carried out at 80-120° only the double bond in the side chain is hydrogenated. At room temperature, 1,4-di-(pyridyl-4')-2,2,3,3-tetracarbethoxybutane is formed in addition to the hydrogenation of the double bond. At 140-160° in ethyl alcohol as well as in methyl alcohol and in dioxane hydrogenation of the pyridine nucleus takes place at the same time as the decarbethoxylation and alkylation of the nitrogen.

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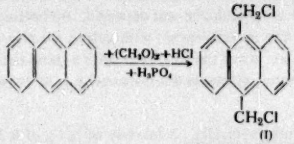
* M. V. Rubtsov gives m.p. 108-109° [2].
** T.p. = C. B. Translation pagination.

CHLOROMETHYLATION OF ANTHRACENE

E. Yu. Gudrinietse and G. Ya. Vanag

Until recently information on the chloromethylation of anthracene was scant [1-3]. Recently this reaction has been studied in detail by M. W. Miller, R. W. Amidon and P. O. Tawney [4]. They prepared 9,10-bis-(chloromethyl)-anthracene (I) by the chloromethylation of anthracene with paraformaldehyde and concentrated hydrochloric acid in dioxane solution and passing hydrogen chloride gas into the reaction mixture at an elevated temperature. The yield of the technical grade product was 65%.

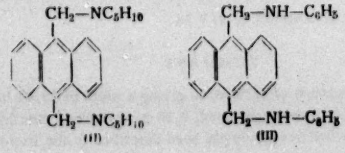
In our work on the chloromethylation of polycyclic compounds [5] we have succeeded in obtaining 9,10-bis-(chloromethyl)-anthracene in 84% yield. The chloromethylation reaction was carried out by a method which had been successfully applied by us previously in the chloromethylation of 2-methylnaphthalene [6], tetralin [7] and chloronaphthalene [8]. Experiments on the chloromethylation of anthracene have shown that this reaction proceeds satisfactorily only within a strictly limited range of temperature (80-85°), and good yields are obtained only when the reaction is started at that temperature and the reaction mixture is vigorously stirred. Under these conditions the reaction is complete within 4-5 hours.



(I)

If the reaction is started at the usual temperature and the mixture is gradually heated to 80-85°, a brown tarry substance is formed from which a small amount of the yellow modification of anthracene together with a small quantity of chloromethylated anthracene can be isolated.

A number of derivatives of 9,10-bis-(chloromethyl)-anthracene have been described [5] which have been obtained by replacing the chlorine atoms by other groups. Our investigations have shown that a chlorine atom in 9,10-bis-(chloromethyl)-anthracene is less reactive than it is, for example, in chloromethyl derivatives of naphthalene. By heating 9,10-bis-(chloromethyl)-anthracene with an excess of piperidine we have obtained 9,10-bis-(piperidinomethyl)-anthracene (II); by heating it with aniline, 9,10-bis-(anilinomethyl)-anthracene (III) was obtained:



(II) (III)

From 9,10-bis-(chloromethyl)-anthracene we have prepared, via the dinitrile, 9,10-anthracenylenediacetic acid, which agreed in its properties with that described in the literature [5]. We have established that the saponification of the nitrile is best carried out in two stages: with dilute sulfuric acid (2:3) to the diamide stage and then with alcoholic alkali to the acid. This cuts the time for hydrolysis from 20 hours (according to the literature) to 10 hours as in our experiments.

EXPERIMENTAL

9,10-Bis-(chloromethyl)-anthracene (I). 35.6 g of anthracene, 22 g of paraformaldehyde, 130 ml of glacial acetic acid, 16.5 ml of 85% or 13.2 g of crystalline phosphoric acid, and 80 ml of concentrated hydrochloric acid were transferred into a 500 ml wide-necked round-bottom flask and the flask was immersed in a water bath at 80-85°. The reaction mixture was heated at this temperature for 4-5 hours with vigorous stirring. The contents were then cooled to room temperature and diluted with 300 ml of water. 9,10-Bis-(chloromethyl)-anthracene was precipitated in the form of a yellow powder. The precipitate was separated, washed with water, then with sodium carbonate and again with water. Yield of the technical product was 46 g (83.9%). In order to remove the last traces of anthracene from the compound the latter was boiled with alcohol and the residue was recrystallized from xylene. The compound was obtained in the form of long greenish-yellow needles. In the course of the determination of the melting point the compound darkened at 262° and melted at 280° (literature: m.p. above 262°; 253-255°). It is insoluble in alcohol and ether, difficultly soluble in benzene and glacial acetic acid, and comparatively soluble in xylene and nitrobenzene.

Found %: Cl 25.55. $C_{17}H_{12}Cl_2$. Calculated %: Cl 25.60.

By oxidizing 9,10-bis-(chloromethyl)-anthracene with chromic anhydride in glacial acetic acid there was obtained 9,10-anthraquinone, m.p. 286°.

When the above mixture of the starting materials was heated gradually to 80-85° under otherwise identical experimental conditions, there was obtained a brown resinous substance which became brittle on cooling. From this substance 5 g of the yellow modification of anthracene was extracted with glacial acetic acid. Yellow crystals, m.p. 213°, were obtained from alcoholic solution (the white modification melts at 216°). On oxidation of the yellow modification 9,10-anthraquinone was obtained. By boiling the brittle substance (obtained after separating the yellow modification of anthracene) with xylene we also succeeded in isolating 8 g (14.7%) of 9,10-bis-(chloromethyl)-anthracene. After the treatment with xylene the residue could not be crystallized. It was easily soluble in benzene, toluene, xylene and nitrobenzene. On evaporating the solution the same resinous product was obtained.

9,10-Bis-(piperidinomethyl)-anthracene (II). A mixture of 2.7 g of 9,10-bis-(chloromethyl)-anthracene and 8.4 g of piperidine was boiled under reflux for 20-30 minutes. The next day it was diluted with water and the residue was recrystallized from a mixture of alcohol and acetone (1:3). Yield 3.5 g (94.6%), in the form of soft, fine, yellow needles, m.p. 204°. The substance is easily soluble in glacial acetic acid, but dissolves with difficulty in mineral acids.

Found %: N 7.52. $C_{26}H_{32}N_2$. Calculated %: N 7.39.

9,10-Bis-(anilinomethyl)-anthracene (III). A mixture of 8.1 g of 9,10-bis-(chloromethyl)-anthracene and 16.8 g of aniline was heated for two hours on a water bath. The next day 60 ml of alcohol was added. The precipitate of 9,10-bis-(anilinomethyl)-anthracene was recrystallized from dioxane. Yield 9.3 g (81.5%). The yellow crystals, m.p. 268°, are insoluble in ether, difficultly soluble in alcohol and mineral acids and readily so in glacial acetic acid. The compound is precipitated by alkalis from its solutions in mineral acids.

Found %: N 7.21. $C_{28}H_{14}N_2$. Calculated %: N 7.34.

SUMMARY

A new method of chloromethylation of anthracene giving a yield of 83.9% has been described and the following derivatives of anthracene have been prepared: 9,10-bis-(piperidinomethyl)-anthracene and 9,10-bis-(anilinomethyl)-anthracene. These had not previously been described in the literature.

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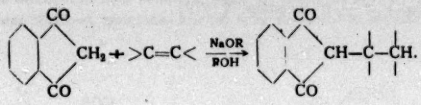
ADDITION OF INDANDIONE-1,3 AND OF ITS NITRO-DERIVATIVE TO A DOUBLE BOND

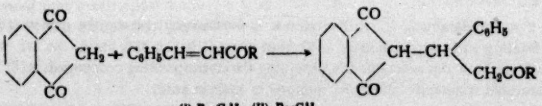
L. Zalukayev

In one of our previous communications [1] we reported that indandione-1,3 adds on to the double bond of chalcone in the presence of sodium alcoholates.

In the present study we have attempted to determine the limits of this reaction. It was found that the reaction occurs only with a sufficiently electrophilic ethylenic bond, with the formation of a 2-substituted derivative of indandione-1,3 according to the equation:

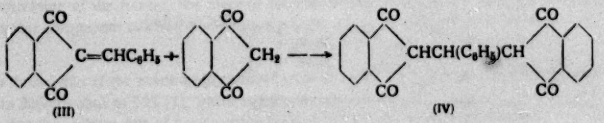


Thus, for example, chalcone gives the addition product 1,3-diphenyl-3-(indandione-1',3'-yl-2')-propanone-1 (I) in 65% yield, while benzalacetone leads to the formation of 4-phenyl-4-(indandione-1',3'-yl-2')-butanone-2 in approximately 40% yield (II):



(I) R=C_6H_5, (II) R=CH_3.

Mesityl oxide does not react at all under these conditions, while, on the other hand, 2-benzylideneindandione-1,3 (III) reacts even without the aid of catalysts and gives benzylidenebisindandione-1,3 (IV) in a yield of 86% of theoretical:

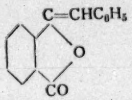


(III) (IV)

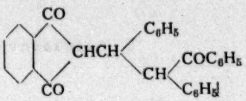
Thus, the reaction gives better yields when the double bond is more electrophilic.

In order to illustrate the more electrophilic character of the double bond in benzylideneindandione as compared with that in chalcone we may mention the reaction with bromine. While chalcone gives a completely stable dibromide [2], 2-benzylideneindandione-1,3 adds on bromine very slowly. The dibromide is unstable and on heating evolves vapors of the halogen, thus resembling in its behavior benzylidene phthalide [3] (V).

From the addition products of indandione prepared by us only benzylidenebisindandione-1,3 has been described [4], which was obtained from the product of addition of desoxybenzoin to benzylideneindandione-1,3 (VI):



(V)

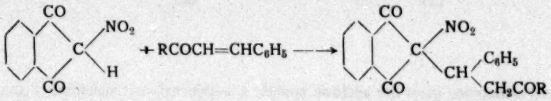


(VI)

The last two compounds required proof of their structure.

To do this, use was made of the reaction of 2-nitroindandione-1,3 with unsaturated compounds.

We obtained two products: 1,3-diphenyl-3-(2'-nitroindandione-1',3'-yl-2')-propanone-1 (VII) and 4-phenyl-4-(2'-nitroindandione-1',3'-yl-2')-butanone-2 (VIII).



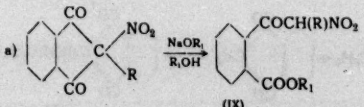
(VII) R=C_6H_5, (VIII) R=CH_3.

The reaction takes place without any catalysts whatsoever on simply refluxing the components in a suitable solvent.

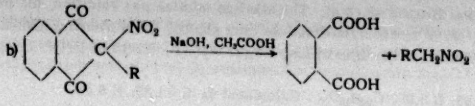
On heating 2-nitroindandione-1,3 with chalcone in methylethyl ketone the compound (VII) is formed in 50% yield, while heating with benzalacetone in alcohol gives (VIII) in 48% yield. So far, when carrying out the reaction in alcohol, we have not succeeded in obtaining the corresponding compounds with 2-benzylideneindandione-1,3, allyl bromide, cinnamic aldehyde, quinone or maleic acid.

It was found that nitration of the addition products of indandione-1,3 to chalcone (I) and benzalacetone (II) proceeds according to the reaction discovered by us earlier [2, 5, 6] and which is general for all 2-substituted indandiones-1,3, and that the nitroindandiones obtained were identical with the nitro-derivatives (VII) and (VIII) obtained from 2-nitroindandione-1,3.

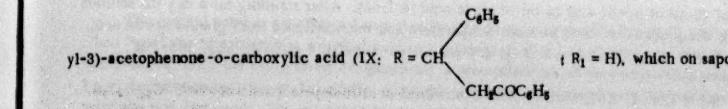
It remained for us to prove the structure of (VII) and (VIII). Earlier we had developed two quite general reactions of 2-nitro-2-substituted indandiones [5, 6]:



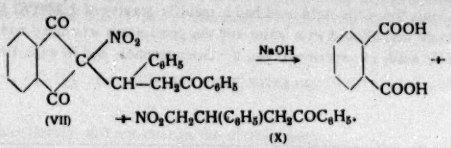
(IX)



Accordingly, the products of addition of 2-nitroindandione-1,3 to chalcone (VII) in the presence of sodium methylate and of sodium ethylate where the ethyl and methyl esters of α-nitro-α-(1,3-diphenyl-propanon-1-

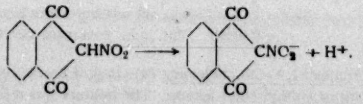


yl-3)-acetophenone-o-carboxylic acid (IX; R = CH ; R_1 = H), which on saponification gave the identical carboxylic acid – an element of their structure, while on hydrolysis of (VII) with caustic alkali 1-nitro-2,4-diphenylbutanone-4 (X) was obtained, which has already been described in the literature [7]:



The structure of the products obtained was thus proved beyond doubt.

G. Vanag [8] showed that 2-nitroindandione-1,3 is an acid which is no less strong than hydrochloric acid. In aqueous solutions it is almost completely dissociated:



This naturally leads to the assumption that addition reactions of 2-nitroindandione-1,3 to chalcone are preceded by ionization of the former, the more so because in the literature the addition of halogens, hydrogen halides and similar compounds is often treated as a process which follows previous ionization of the attacking molecule.

We have found that if the reaction is carried out in benzene, the yield of the nitrodiketone amounts to 25-40%, and in 90% alcohol to 20% [1], while in 80% alcohol the reaction does not proceed at all. It is also characteristic that the sodium salt of 2-nitroindandione-1,3 does not react with chalcone.

These facts give reason to assume, with the usual caution, that 2-nitroindandione-1,3 takes part in the reaction without preliminary disscciation, although the reaction apparently possesses a heterolytic character.

EXPERIMENTAL

Interaction of indandione-1,3 with chalcone. 42 g of indandione-1,3 and 60 g of chalcone was dissolved in 500 ml of 3% sodium methylate in methanol. The deep red solution was allowed to stand for a day after which the precipitate was filtered off (8 g). The alkaline solution was acidified, the precipitate separated and air-dried. Yield 83 g. After two recrystallizations from alcohol 1,3-diphenyl-3-(indandione-1',3'-yl-2')-propanone-1 (I) was obtained in the form of large whole crystals. Yield 64 g (63%) m.p. 128-129°.

Found %: C 81.23; H 5.09. $C_{24}H_{18}O_3$. Calculated %: C 81.36; H 5.08.

Compound (I) dissolves in alkalis giving rise to an intense red color. It is precipitated from the alkaline solution by acidification in the form of a white powder. It crystallizes excellently from glacial acetic acid and alcohol. When refluxed with the latter it produces a faint red coloration.

Nitration of (I). 13 g of the triketone was dissolved in 250 ml of glacial acetic acid. To the solution was added a mixture of 25 ml of acetic and 25 ml of nitric acid (d 1.52). After standing for a day the solution was diluted with water, the precipitate dried at room temperature and recrystallized from glacial acetic acid. Yield of 1,3-diphenyl-3-(2'-nitroindandione-1',3'-yl-2')-propanone-1 (VII), 8 g (54%). M.p. 169-170°.

Found %: C 72.38; H 4.33; N 3.61. Mol.wt. 389 (determined ebullioscopically in acetone). $C_{24}H_{17}O_5N$. Calc. %: C 72.18; H 4.21; N 3.51. Mol. wt. 399.

The table gives data from some other variations of the nitration procedure which were carried out by heating on the water bath to incipient evolution of oxides of nitrogen, after which the mixture was left standing at room temperature. In all cases the nitric acid used had a specific gravity of 1.38. At the end of the period shown in the table the mixture was diluted with water and the precipitate was dried and recrystallized; in experiment No. 1 – from acetic acid; in experiment No. 2 – from alcohol; and in experiment No. 3 it was washed with hot alcohol.

Expt. no.	Amount of triketone (g)	Amount of acetic acid (ml)	Amount of nitric acid (ml)	Reaction time	Yield of nitro-derivative (%)	Melting point
1	16	150	50	12 hours	55	167—168°
2	10	100	50	10 min.	62	160—167
3	34	300	150	10 "	65	164—166

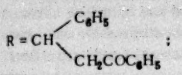
Interaction of 2-nitroindandione-1,3 with chalcone. (a) 15 g of 2-nitroindandione-1,3 and 14 g of chalcone were mixed with 100 ml of methyl ethyl ketone. The mixture was refluxed on a water bath for one hour after which it was diluted with water. The separated oily product quickly solidified. After refluxing with alcohol, a white crystalline powder of 1,3-diphenyl-3-(2'-nitroindandione-1',3'-yl-2')-propanone-1 (VII) was obtained, m.p. 169-170°. Yield 50%. A mixture of the substance with that obtained by nitration of (I) melted without depression.

(b) 22.7 g of 2-nitroindandione-1,3 and 21 g of chalcone were refluxed in 200 ml of benzene for 4 hours. The compounds dissolved gradually on refluxing, but towards the end of the reaction there separated a small amount of a greasy precipitate. The benzene layer was decanted and half of the solvent removed, but on cooling no crystallization took place. After evaporation of the remaining benzene a small amount of alcohol was added

to the greasy residue, the crystals were filtered off and recrystallized from alcohol. M.p. 165-168°. The yield of (VII) varied in different experiments from 35 to 40%.

(c) 23 g of 2-nitroindandione-1,3 and 26 g of chalcone were dissolved in a mixture of 350 ml of ethanol and 50 ml of water. After heating the mixture on a boiling water bath for 1½ hours and cooling, crystals of unchanged chalcone, m.p. 58°, separated in an amount nearly equal to that taken originally. Formation of the adduct (VII) could not be established.

The action of alcoholates on the nitrotriketone. (a) 5 g of nitrotriketone (VII) was treated with 50 ml of 3% sodium methylate. After acidification and dilution of the mixture with water the precipitate of the methyl ester of α-nitro-α-(1,3-diphenyl-propanon-1-yl-3)-acetophenone-o-carboxylic acid (IX:

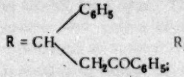


; $R_1 = CH_3$) was separated, dried and recrystallized from alcohol. Yield 4.3 g (80%), m.p. 155-156°.

Found %: C 70.09; H 4.82; N 3.63. $C_{25}H_{21}O_6N$. Calculated %: C 69.61; H 4.87; N 3.25.

The methyl ester is also formed in a similar way in aqueous-alcoholic alkali, although the yield is lower. When 7 g of the nitrotriketone was dissolved in a mixture of 50 ml of caustic soda and 30 ml of methanol, there was obtained, after the same series of operations, a precipitate which on recrystallization from benzene gave 3 g of a substance melting at 155-156°. When this substance was mixed with that obtained above the melting point was not depressed. The substance is very soluble in benzene and moderately soluble in alcohol.

(b) 5 g of the nitrotriketone was dissolved in 100 ml of 3% sodium ethylate in ethyl alcohol. The substance dissolved rapidly giving rise to a reddish coloration. After 5 minutes the reaction mixture was diluted with water and acidified with hydrochloric acid. The white precipitate was separated, dried and recrystallized from alcohol. There was obtained 4.2 g (75%) of colorless crystals of the ethyl ester of the carboxylic acid (IX:



$R_1 = C_2H_5$), m.p. 146-148°. Recrystallization from glacial acetic acid from which the substance crystallizes excellently, did not change the melting point.

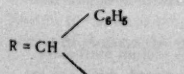
Found %: C 69.95; H 5.24; N 3.66. $C_{26}H_{23}O_6N$. Calculated %: C 70.12; H 5.16; N 3.15.

In a manner similar to that described under (a) there formed, from 7 g of the nitrotriketone treated with a mixture of 50 ml of alcohol and 50 ml of 10% caustic soda, approximately 3 g of the ethyl ester, m.p. 144-145°.

(c) 10 g of the nitrotriketone was dissolved in sodium methylate and the solution was acidified. The ester was separated and dissolved in hot 5% sodium hydroxide solution. The mixture was again made acid, the precipitate of the carboxylic acid separated and the crude product rapidly dissolved in glacial acetic acid. On standing a white crystalline powder separated, m.p. 168°. Yield 9 g.

Found %: N 3.45. $C_{24}H_{19}O_6N$. Calculated %: N 3.36.

The substance dissolves in sodium bicarbonate solution at room temperature. Experimental data conform to the formula of α-nitro-α-(1,3-diphenyl-propanon-1-yl-3)-acetophenone-o-carboxylic acid (IX), where



; $R_1 = H$.

Hydrolysis of the nitro-derivative in the presence of sodium hydroxide. 6 g of the nitrotriketone, m.p.

166-167° (VIII), was placed in a solution of 1 g of sodium hydroxide in 50 ml of water (ca. 3 moles of alkali per 1 mole of the substance) and the mixture was refluxed for 15 minutes. On cooling, yellow oily droplets were suspended in the liquid; these solidified quickly. The white powder was separated and recrystallized from alcohol. M.p. 100-102°. The yield of 1-nitro-2,4-diphenylbutanone-4 (X) was 1.5 g (36%). The substance is in the form of a colorless crystalline powder and is easily soluble in acetic acid and alcohol.

Found %: C 71.50; H 5.85; N 5.37. $C_{16}H_{15}O_3N$. Calculated %: C 71.37; H 5.58; N 5.21.

Interaction of indandione-1,3 with benzalacetone. 11 g of benzalacetone was dissolved in 50 ml of ethanol. To this solution there was added 10 g of indandione-1,3, followed by 75 ml of 3% sodium methylate in methanol. After refluxing for 10 minutes the mixture was diluted with water, filtered and acidified. The separated yellow oil crystallized. After washing with alcohol, the crystalline powder was filtered off and dried. Yield of 4-phenyl-4-(indandione-1',3'-yl-2')-butanone-2 (II), 9 g. M. p. 106°. After several recrystallizations from alcohol the substance melted at 113-114°.

2 g of the substance melting at 106° was dissolved in a mixture of 30 ml of glacial acetic acid and 30 ml of nitric acid (d 1.39). After warming to 30-35° the solution was allowed to stand for a day and then diluted with water, and the precipitate was separated and recrystallized from warm acetic acid. M. p. 167-168°. White crystals of 4-phenyl-4-(2'-nitroindandione-1',3'-yl-2')-butanone-2 (VII).

Found %: C 67.66; H 4.45; N 4.14. $C_{19}H_{15}O_5N$. Calculated %: C 67.98; H 4.64; N 4.15.

Interaction of 2-nitroindandione-1,3 with benzalacetone. 7.3 g of freshly distilled benzalacetone and 9.55 g of 2-nitroindandione-1,3 were refluxed in 50 ml of alcohol on a water-bath for 40 minutes. After standing for several hours the colorless crystals were filtered off, m.p. 166-167°. Yield 4-phenyl-4-(2'-nitroindandione-1',3'-yl-2')-butanone-2 (VIII), 8 g (48%), based on benzalacetone. A mixture with the substance obtained in the foregoing experiment by direct nitration of the product of addition of indandione to benzalacetone, melted without depression at 166-167°.

Found %: N 4.12. $C_{19}H_{15}O_5N$. Calculated %: N 4.15.

The yields of the substance were not always constant and in individual cases exceeded 60%. On refluxing in acetic acid the substance undergoes a change, the solution assumes a green color and the melting point is lowered.

On refluxing with alkalis the odor of bitter almonds was noticeable. On cooling, a small amount of colorless crystals of 4-phenyl-5-nitro-pentanone-2, m.p. 95-96°, could be isolated.

Found %: N 6.39. Mol.wt. 191 (by Rast's method). $C_{11}H_{13}O_3N$. Calculated %: N 6.77. Mol.wt. 207.

The substance was not investigated further.

Interaction of 2-benzylideneindandione-1,3 with indandione-1,3. (a) 3.1 g of indandione-1,3 and 5 g of 2-benzylideneindandione-1,3 were dissolved in 100 ml of alcohol and refluxed on a water bath for 30 minutes. Separation of the reaction product could be observed even during the refluxing period. After cooling, the grey precipitate was filtered off and washed with alcohol. M.p. 162-163° (dec.). Yield of 2-benzylidenebis-indandione-1,3 (IV), 7 g (86%).

Found %: C 78.74; H 4.56. $C_{25}H_{16}O_4$. Calculated %: C 78.94; H 4.21.

The substance dissolves easily in aqueous alkalis with a reddish coloration characteristic of derivatives of indandione. On refluxing with alkalis the odor of benzaldehyde can be perceived.

(b) 9 g of indandione-1,3 and 3.3 ml of benzaldehyde were added to 100 ml of 3% sodium methylate. After refluxing the mixture for 5 minutes and diluting with water, the precipitate was separated, dried and recrystallized from glacial acetic acid, m.p. 162-164°. Yield 6.7 g.

Nitration of benzylidenebisindandione-1,3. 3 g of benzylidenebisindandione-1,3 (IV) (m.p. 162-164°) was dissolved in 250 ml of glacial acetic acid, and to the solution was added 15 ml of nitric acid (d 1,52). After standing for a day the solution was poured into water, the precipitate separated and dried and recrystallized from glacial acetic acid. Yield of dinitrobenzylidenebisindandione-1,3, 2 g (54%). Colorless crystalline powder, m.p. 178-179°. On heating to the melting temperature the substance decomposes vigorously with the evolution of oxides of nitrogen.

Found %: C 63.98; H 3.18; N 5.89. $C_{25}H_{14}O_8N_2$. Calculated % C 63.87; H 2.98; N 5.96.

Bromination of 2-benzylideneindandione-1,3. 3 g of the benzylidene derivative (III) (m.p. 151-152°) was dissolved in glacial acetic acid. To the solution was added the calculated amount of bromine in the same solvent. The color of bromine disappeared only after several hours. The white crystalline precipitate was separated. Yield 3 g. After recrystallization from acetic acid – with a vigorous evolution of bromine vapors – there was obtained 2-benzylideneindandione-1,3 dibromide, m.p. 171-172°.

Found %: Br 40.28. $C_{18}H_{10}O_2Br_2$. Calculated %: Br 40.68.

On gentle warming in 3% sodium methylate the substance loses bromine and changes into a product of m.p. 153-154° which melts without depression when mixed with the original compound (III).

Other unsaturated compounds and derivatives of indandione-1,3. (a) 5 g of 2-nitroindandione-1,3 and 2,5 ml of allyl bromide were heated on a water bath with 50 ml of ethyl alcohol for 2 hours. After removing 40 ml of alcohol the red-colored solution was diluted with water. There separated an oil which rapidly changed to a crystalline slurry. After washing with alcohol and recrystallizing twice from acetic acid there were obtained white crystals of the ethyl ester of α-nitroacetophenone-o-carboxylic acid [9], m.p. 83-84°. The substance did not depress the melting point of an authentic sample.

(b) 2.34 g of 2-benzylideneindandione-1,3 and 1.91 g of 2-nitroindandione-1,3 were refluxed in 50 ml of alcohol for 1 hour. The initially yellow-colored liquid gradually became lighter. The reaction mixture was cooled, and yellow crystals of the original benzylideneindandione separated. Yield 2 g, m.p. 151-152°. When mixed with an authentic sample the substance melts without depression. From the alcoholic mother liquor it is possible to isolate the ethyl ester of α-nitroacetophenone-o-carboxylic acid which melts at 82-83° after two recrystallizations from alcohol.

(c) 3.86 g of 2-nitroindandione-1,3 and 2.6 g of cinnamaldehyde were refluxed in 15 ml of alcohol for 1 hour. No crystallization took place on cooling. On diluting with water there separated a viscous non-crystallizable oil which decomposed on slight warming. When the oil was dissolved from alcohol and an alcoholic solution of phenylhydrazine was added, a precipitate formed. The latter is not cinnamaldehyde phenylhydrazone, but rather phenylhydrazine nitroindandionate. The substance is difficult to purify. Attempts to determine the melting point of the deep-red precipitate obtained by recrystallization from alcohol failed because the substance decomposed each time. No further investigations were undertaken.

Found %: N 14.48. $C_6H_8N_2 \cdot C_9H_8O_4N$. Calculated %: N 14.05.

Under similar conditions, using quinone and maleic acid, the individual condensation products could not be obtained. In the case of quinone a polymeric substance was obtained, and in the case of maleic acid the ethyl ester of α-nitroacetophenone-o-carboxylic acid [9].

(c) 8 g of indandione-1,3 was dissolved in 70 ml of 3% sodium methylate and the mixture added to a solution of 5.4 g of mesityl oxide in 50 ml of ethanol. After standing for 3 hours the original indandione-1,3 was the only product which separated from the solution. Yield 2.5 g. Refluxing of a mixture of the same components in the same proportions for 15 minutes gave bindone, m.p. 206-207°. When mixed with an authentic sample of bindone the substance did not depress the melting point.

SUMMARY

The addition reaction of indandione-1,3 and of 2-nitro-indandione-1,3 to some unsaturated compounds has been described. The structure of the compounds obtained has been proved.

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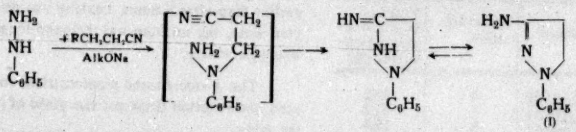
REACTIONS OF HYDRAZINE DERIVATIVES

IX. INTERACTION OF PHENYLHYDRAZINE WITH β-SUBSTITUTED PROPIONITRILES

A. N. Kost and V. V. Ershov

It has been observed previously that in basic media β-alkoxypropionitriles easily exchange their alkoxy group for that of another alcohol [1], an amino-group or a hydrocarbon radical [2, 3]. β-thiopropionitriles react in a similar way, and the exchange of the chlorine in β-chloropropionitrile takes place with particular ease [1]. In the case of β-aminopropionitriles the exchange of the amino-group is more difficult [2]. If, however, β-aminopropionitrile is transformed into the corresponding hydroxide of the quaternary ammonium base, the amino group becomes very reactive [4, 5].

In the present study we have investigated the reaction of different β-substituted propionitriles with phenylhydrazine (in the presence of sodium alcoholate) giving rise to the formation of 3-amino-1-phenylpyrazoline (I) in varying yields depending on the nature of the substituent and the conditions of experiment.



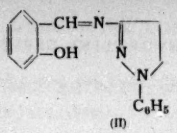
R=Cl, HO, C_2H_5O, C_4H_9O, $(CH_3)_2N$, $(C_2H_5)_2N$.

3-Amino-1-phenylpyrazoline was obtained previously by Duffin and Kendall [6] by the interaction of phenylhydrazine with acrylonitrile.

We have found that the reaction proceeds best with β-dimethylaminopropionitrile and less satisfactorily with β-chloro- and β-alkoxypropionitriles (see table). In the case of β-hydroxypropionitrile the interaction with phenylhydrazine is complicated by hydrolysis by the water formed in the reaction. These facts have already been observed earlier in reactions with β-substituted propionitriles [1, 2]. Of essential importance here is the solvent which raises the boiling point of the mixture and may, in addition, take part in the reaction. β-ethoxypropionitrile splits off its alkoxy group more easily than β-butoxypropionitrile (the yields are higher in the former case). If, however, β-butoxypropionitrile is reacted in ethyl alcohol as the solvent, the yield is considerably higher because the exchange of alkoxy groups takes place more easily in basic solvents. By contrast, β-ethoxypropionitrile in butyl alcohol gives, for these very reasons, lower yields than in ethyl alcohol. The reverse effect was observed in the case of β-dialkylaminopropionitriles, where the use of butyl alcohol, rather than ethyl alcohol, gave higher yields. In these compounds the free pair of electrons on the nitrogen compensates the polarization of the bond due to the nitrile group, as a result of which exchange of the substituent on the β-carbon atom in basic solvents is more difficult than in the case of alkoxynitriles. In this case an increase of the boiling point of the solvent facilitates the reaction with phenylhydrazine because under these conditions the amino group splits off more easily. Substitution of the amino group by the alkoxy group under these conditions hardly occurs. This has been confirmed by us by a special experiment, i.e., by heating

β-diethylaminopropionitrile with sodium butylate in butyl alcohol (refluxing for 8 hours), the aminonitrile remaining unchanged and no β-butoxypropionitrile could be detected.

By reacting 3-amino-1-phenylpyrazoline (I) with salicylaldehyde we prepared the salicylalimine (II) of this aminopyrazoline, which gives an insoluble complex with salts of copper oxide:



(II)

Acylation of 3-aminopyrazoline gave 3-acetylamino-1-phenylpyrazoline in higher yield than that given in the literature [6].

The compounds prepared have been characterized by their absorption spectra.*

EXPERIMENTAL

3-Amino-1-phenylpyrazoline (I). 0.5 g of metallic sodium was dissolved in 20 ml of alcohol and to the solution was added 10.8 g (0.1 mole) of phenylhydrazine and 0.1 mole of a β-substituted propionitrile. The mixture was refluxed for 8 hours. On cooling, 3-amino-1-phenylpyrazoline precipitated. This was filtered off, washed with water and ethyl alcohol and recrystallized from alcohol, m.p. 169°. Literature m.p. 169° [6]. The absorption spectrum of the substance in methyl alcohol has a maximum at λ_{max} 276 mμ.

Substituent R in the formula RCH_2CH_2CN	Solvent	Refluxing time	Yield of 3-amino-1-phenylpyrazoline (%)
Cl*	C_2H_5OH	8	53.2
HO	C_2H_5OH	8	37.2
HO	C_4H_9OH	8	19.3
C_2H_5O	C_2H_5OH	8	63.3
C_2H_5O	C_4H_9OH	8	57.7
p-C_4H_9O	C_2H_5OH	8	65.2
p-C_4H_9O	C_4H_9OH	8	52.8
$(CH_3)_2N$	C_2H_5OH	14	22.5
$(CH_3)_2N$	C_4H_9OH	5.5	87.0
$(C_2H_5)_2N$	C_4H_9OH	6	22.4

* An additional amount of sodium was used to neutralize the hydrogen chloride formed.

If the precipitate of aminopyrazoline was formed earlier than after 8 hours, heating was discontinued, and vice versa, the mixture was refluxed longer than 8 hours where necessary.

The β-substituted propionitriles and the solvent used, the reaction time and the yield of (I) are listed in the table.

3-acetylamino-1-phenylpyrazoline. To 50 ml of acetic anhydride was added 50 g of pyrazoline (I). The mixture was stirred for one hour, diluted with water and the precipitate of 3-acetylamino-1-phenylpyrazoline filtered off. Yield 24 g (40.3%), m.p. 192°. Duffin and Kendall give a yield of 15%, m.p. 192° [6]. The absorption spectrum of the substance in methyl alcohol exhibits maxima at λ_{max} = 252.5 and 298 mμ.

3-Salicylalimine-1-phenylpyrazoline. A mixture of the pyrazoline (I) (5.7 g, 0.035 mole), salicylaldehyde (4.27 g, 0.035 mole) and 40 ml of ethyl alcohol was refluxed for one hour. The precipitate of bright red crystals was filtered off and recrystallized from a fairly large amount of alcohol. Yield 5.5 g (60%). m.p. 128° (decomp.). The absorption spectrum in methyl alcohol exhibits maxima at λ_{max} =262 and 432 mμ.

Found % N 15.55, 15.66. Calculated on $C_{16}H_{15}ON_3$. N 15.82.

The salicylalimine obtained reacts easily with salts of copper oxide forming a difficultly soluble brown copper complex, m.p. 145° (decomp.).

* The spectra were recorded by N. B. Kupletskaya.

SUMMARY

The authors have investigated the reaction of β-substituted propionitriles with phenylhydrazine leading to the formation of 3-amino-1-phenylpyrazoline.

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REACTIONS OF HYDRAZINE DERIVATIVES

X. ABSORBPTION SPECTRA OF AZINES AND PYRAZOLINES

N. B. Kupletskaya, A. N. Kost and I. I. Grandberg

In previous papers [1-4] we have described the synthesis of a number of aldo- and ketoazines as well as their rearrangement into pyrazoline bases by the action of formic and oxalic acids. Having prepared a whole series of such compounds we have recorded ultra-violet absorption spectra of azines and pyrazolines and of their hydrochlorides and N-formyl derivatives.

All the aldoazines investigated have an absorption band in the region below 225 mμ (Fig. 1), which is in agreement with the literature [5].

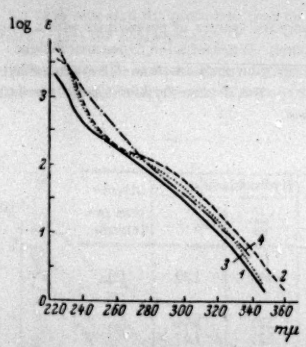


Fig. 1. Absorption spectra of aldoazines. 1) acetaldazine, 2) butyraldazine, 3) isobutyraldazine, 4) isovaleraldazine.

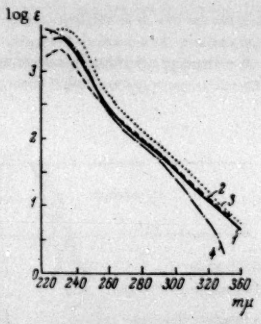


Fig. 2. Absorption spectra of ketoazines. 1) methylethylketoazine λ_{max} 230 mμ, log ε 3.45. 2) methylpropylketoazine, λ_{max} 230 mμ, log ε 3.32, 3) cyclohexanoneazine λ_{max} 230 mμ, log ε 3.60, 4) acetonehexanoneazine.

In the case of the ketoazines the maximum of the absorption band lies about 230 mμ (Fig. 2), with the exception of the mixed azine of cyclohexanone and acetone where the maximum lies in a shorter wave-length region.

In the case of most of the pyrazolines investigated two absorption bands are found: an intensive one in the region 225-230 mμ (log ε 3,5) and a less intensive one (log ε 1-2) in the region 320 to 330 mμ (Figs. 3, 4, and table). The maxima of the short-wave region of 5- methylpyrazoline and 3,4-trimethylene-5,5-tetramethylenepyrazoline (I) lie below 225 mμ. In the case of 5 - methylpyrazoline a weak absorption band appears, in addition, in the region around 380 mμ. The spectrum of 4,4-dimethyl-5-isopropylpyrazoline is characterized by a very indistinct band in the region 300-330 mμ lacking a definite maximum. A distinctly characteristic spectrum is that of 3,4-tetramethylene-5,5-pentamethylenepyrazoline having only one absorption band with a maximum at 231 mμ (Fig. 4).

As we pass from pyrazolines to their hydrochlorides no distinct relationship in the change in corresponding absorption spectra can be found. In most cases the intensity of absorption is lowered, especially in the short-wave region of the spectrum (Fig. 5, table). The absorption curves of the hydrochlorides of 4-isopropyl-5-isobutylpyrazoline and 3,4-trimethylene-5,5-tetramethylenepyrazoline differ little from the spectra of the pyrazolines themselves. In the case of the hydrochlorides of 4-methyl-5-ethylpyrazoline and 3,4-tetramethylene-5,5-pentamethylenepyrazoline an absorption band appears in the region 270-280 mμ (Fig. 5).

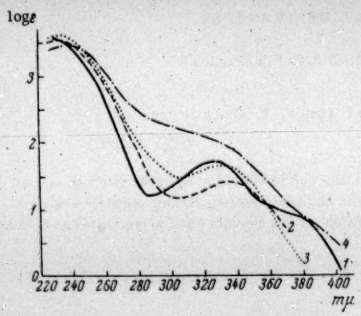


Fig. 3. Absorption spectra of 5-alkylpyrazoline: 1) 5-Methylpyrazoline; 2) 4-methyl-5-ethylpyrazoline; 3) 4-isopropyl-5-isobutylpyrazoline; 4) 4,4-dimethyl-5-isopropylpyrazoline.

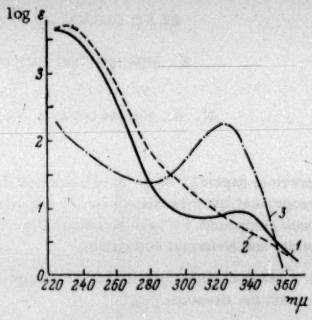


Fig. 4. Absorption spectra of pyrazolines with a spirocyclic structure. 1) 3-Methyl-5,5-pentamethylenepyrazoline; 2) 3,4-tetramethylene-5,5-pentamethylenepyrazoline; 3) 3,4-trimethylene-5,5-tetramethylenepyrazoline.

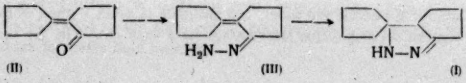
Pyrazoline	Base		Hydrochloride		Literature reference
	λ_{max} mμ	log ε	λ_{max} mμ	log ε	
5-Methyl-	326	1.69	310	1.33	[2]
1-Formyl-5-methyl-	317	1.19	—	—	[2]
4-Methyl-5-ethyl-	232 336	3.52 1.40	227 327	2.94 1.67	[2]
4-Isopropyl-5-isobutyl-	231 331	3.60 1.66	228 333	2.97 1.45	[2]
4,4-Dimethyl-5-isopropyl-	234	3.45	231	3.18	[2]
1-Formyl-4,4-dimethyl-5-isopropyl-	236	4.08	—	—	[2]
1-Acetyl-4,4-dimethyl-5-isopropyl-	242	4.08	—	—	[2]
1,4,4-Trimethyl-5-isopropyl-	232	3.54	—	—	[4]
1-Formyl-5-methyl-3,5-dipropyl	233	4.18	—	—	[3]
3-Methyl-5,5-pentamethylene-	228 333	3.64 0.95	243	2.21	[3]
3,4-Tetramethylene-5,5-pentamethylene-	231	3.70	274	2.44	[6]
1-Formyl-3,4-tetramethylene-5,5-pentamethylene-	237	4.23	—	—	[1]
3,4-Trimethylene-5,5-tetramethylene	324	2.24	323	1.56	[*]

* Described in this paper.

The absorption spectra of N-substituted pyrazolines show that the shape of the curve depends little on the nature of the substituents (Fig. 6, table). As the methyl group is exchanged for the formyl and acetyl groups the maximum of the short-wave band is slightly displaced towards the red end of the spectrum, as in the case of N-derivatives of 4,4-dimethyl-5-isopropylpyrazolines (Fig. 6, Table). The absorption band of N-derivatives in the region 320-330 mμ is less pronounced than in the case of the corresponding pyrazolines with a free NH-group.

At first we intended to prepare 3,4-trimethylene-5,5-tetramethylenepyrazoline (I) by rearrangement of cyclopentanoneazine. It was found, however, that this azine, unlike cyclohexanoneazine [6], is transformed by the action of oxalic or acetic acid into a more complex compound (m.p. 140°). For this reason the necessary pyrazoline (I) was synthesized by a different method.

N. D. Zelinsky and N. I. Shuikin [7] prepared the hydrazone (III) by the action of hydrazine hydrate on a cold alcoholic solution of cyclopentylidenecyclopentanone (II). On heating with alkali this hydrazone apparently underwent cyclization into the pyrazoline (I), because after splitting off nitrogen, Zelinsky and Shuikin did not obtain an olefine, but a cyclopropanhydrocarbon.



(II) (III) (I)

We have repeated the procedure used by the above authors and, having isolated the hydrazone (III), we transformed it into the pyrazoline (I).

If the ketone (II) is acted upon with hydrazine hydrate in butyl alcohol at 130°, the pyrazoline (I) may be obtained in good yield without the necessity of isolating the hydrazone (III).

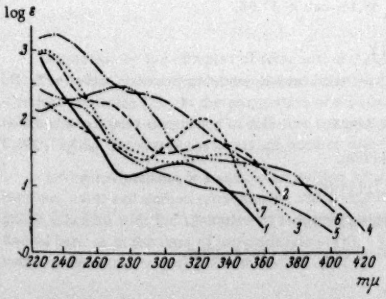


Fig. 5. Absorption spectra of pyrazoline hydrochloride. 1) 5-methylpyrazoline, 2) 4-methyl-5-ethylpyrazoline, 3) 4-isopropyl-5-isobutylpyrazoline, 4) 4,4-dimethyl-5-isopropylpyrazoline, 5) 3-methyl-5,5-pentamethylenepyrazoline, 6) 3,4-tetramethylene-5,5-pentamethylenepyrazoline, 7) 3,4-trimethylene-5,5-tetramethylenepyrazoline.

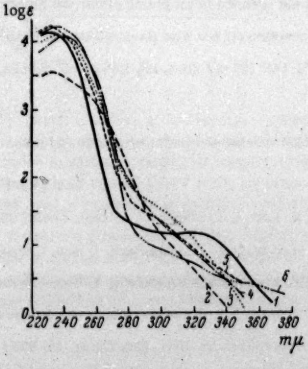


Fig. 6. Absorption spectra of 1-acyl-pyrazolines. 1) 1-formyl-5-methylpyrazoline, 2) 1-methyl-4,4-dimethyl-5-isopropylpyrazoline, 3) 1-formyl-4,4-dimethyl-5-isopropylpyrazoline, 4) 1-acetyl-4,4-dimethyl-5-isopropylpyrazoline, 5) 1-formyl-5-methyl-3,5-dipropylpyrazoline, 6) 1-formyl-3,4-tetramethylene-5,5-pentamethylenepyrazoline.

EXPERIMENTAL

The absorption spectra were recorded with the spectrophotometer SF-4. In all cases the solvent was methyl alcohol. To record the spectra of the hydrochlorides methyl alcohol containing some concentrated hydrochloric acid was used as solvent. In view of the ease with which they undergo oxidation all the azines and pyrazolines were investigated after being freshly prepared. In particular this concerns pyrazolines which have no substituent in position 3, because these compounds eliminate nitrogen even at room temperature.

Cyclopentylidenecyclopentanone (II) was prepared by heating 197 g of cyclopentanone and 96 g of calcium carbide in a Soxhlet apparatus, of 250 ml capacity, for four hours (one drainage every two minutes). After extracting the residue with ether, followed by distillation, there was obtained 95 g (54%) of the ketone (II).

B.p. 119-122° (14 mm) 136-137° (25 mm), n_D^{20} 1.5209; d_4^{20} 1.0169, MR_D 44.97; calcd. 43.52; ΔMR_D 1.45.

Literature: b.p. 116-118° (10 mm), n_D^{20} 1.5211, d_4^{20} 1.0172 [7].

The hydrazone (III) was obtained by adding 10 g of 96% hydrazine hydrate to a solution of 20 g of the ketone (II) in 10 ml of ethyl alcohol. After standing for one day at room temperature, white flakes of the hydrazone (III) were precipitated quantitatively which after recrystallization from alcohol had an m.p. of 90-91° [7].

The substance is easily soluble in alcohol and water, and insoluble in ether. When wetted with alcohol the substance did not show any signs of decomposition after storage for a fortnight. The dry compound decomposes quickly on exposure to air.

3,4-Trimethylene-5,5-tetramethylenepyrazoline (I). A mixture of 30 g (0.2 mole) of ketone (II), 15 ml of butyl alcohol and 11.4 g (0.22 mole) of 96% hydrazine hydrate was refluxed for 6 hours and distilled in vacuo. There was obtained 31.4 g (95.7%) of pyrazoline (I), b.p. 141-144° (22 mm).

The fraction boiling at 142° (21 mm) has n_D^{20} 1.5024, d_4^{20} 1.0049, MR_D 48.24; calcd. 47.65.

Found %: N 16.96, 17.09. $C_{10}H_{18}N_2$. Calculated %: N 17.05.

We did not succeed in preparing either the picrate or the nitro-derivative in a crystalline state.

The pyrazoline (I) was also prepared by refluxing the hydrazone (III) in butyl alcohol for six hours. Yield 68%.

B.p. 140-145° (21-22 mm); n_D^{20} 1.5017, d_4^{20} 1.0062, MR_D 48.14; calcd. 47.65.

SUMMARY

Absorption spectra of a series of azines and pyrazolines have been investigated.

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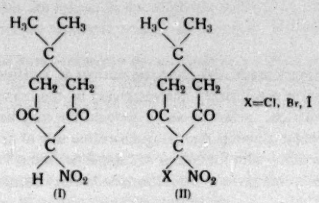
HALOGEN DERIVATIVES OF NITRODIMEDONE

O. Ya. Neiland, E. Yu. Gudrinietse and G. Ya. Vanag

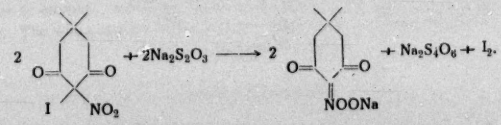
We have recently shown [1] that nitrodimedone (4-nitro-1,1-dimethylcyclohexanedione-3,5) (I) in aqueous solution is easily chlorinated and brominated with the formation of chloro-and bromonitrodimedones (II). Iodonitrodimedone cannot be obtained in this way. We have prepared it in 40% yield by the nitration of iododimedone [2] with fuming nitric acid in glacial acetic acid solution. Iodonitrodimedone may be obtained in almost quantitative yield (92%) by the action of the complex compound formed by iodine monochloride and dioxane on nitrodimedone in acetic acid solution.



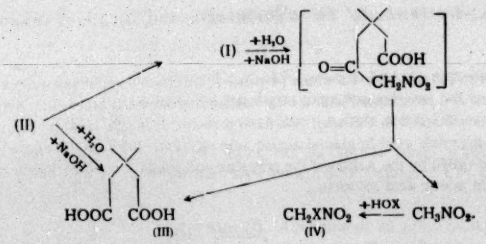
(I) (II)

Iodination by the complex of composition $C_4H_8O_2 \cdot ICl$ [3] was first used by A. P. Terentyev and coworkers [4]. The iodine monochloride was prepared from iodine and sulfuryl chloride in the presence of anhydrous aluminum chloride [5]. In the preparation of the above complex in carbon tetrachloride solution, however, we obtained a complex compound of different composition, differing from that described in the literature, namely, $C_4H_8O_2 \cdot I_2Cl_2$. It crystallized as orange needles with m.p. 103°, and is apparently an excellent iodinating agent.

Iodonitrodimedone is a yellow crystalline substance. It does not dissolve in water but dissolves readily in benzene, ether and carbon tetrachloride and is slightly soluble in glacial acetic acid. It dissolves in potassium iodide solutions with the liberation of iodine. It is possible that the same complex compounds are being formed here as in the case of nitroindandione [6]. In sodium thiosulfate solution iodonitrodimedone liberates iodine in the same way as iodonitroindandione [7]:



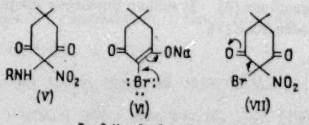
The Halogen derivatives of nitrodimedone (II) show a series of characteristic reactions. They react with water splitting off hypochlorous, hypobromous and hypoiodous acids. In alkaline solutions oxidations takes place and the solutions acquire a deep color: chloronitrodimedone gives this coloration even at room temperature, bromo-nitrodimedone on heating, and iodonitrodimedone only on boiling. It is possible to isolate from the acidified solution some nitrodimedone (I), β,β-dimethylglutaric acid (III) and a compound with lachrymatory properties which is evidently halogenated nitromethane (IV). Analogous products are obtained from the action of sodium hypochlorite or hypobromite on nitrodimedone. The reaction evidently takes place in the following way:



Bromo-and iodonitrodimedones react with aromatic amines in a different way from chloronitrodimedone. The aniline salt of nitrodimedone is precipitated quantitatively by the reaction of excess aniline on bromo- or iodonitrodimedone in ether solution. p-Bromo-and p-iodoaniline may be isolated from the solution. If the reactants are taken in equimolecular amounts the halogenoaniline salt of nitrodimedone is obtained in 60% yield. Analogous reactions take place with toluidines and napthylamines, but nitroanilines, aminobenzoic acids and aminophenols do not react with bromo-and iodonitrodimedones; benzidine and o-phenylenediamine are oxidized.

Chloronitrodimedone gives two series of compounds with aromatic amines: one soluble in alkaline carbonates and ammonia (V) and one insoluble. The nature of the latter has not yet been discovered, since they are obtained in small amount and are difficult to isolate in the pure state.

The halogen atom in halogenodimedones is firmly bound and is not split off even on boiling with alkali [2]. This may be explained by the effect of the conjugation between the double bond of the enol form and the free pair of electrons on the halogen (VI), as a result of which the halogen atom is deactivated [8]:



$R = C_6H_5, CH_3C_6H_4, C_{10}H_7.$

A nitro group in the halogenodimedones prevents enolization and at the moment of reaction with a nucleophilic reagent a conjugated system of σ-π-bonds is formed as a result of which the halogen becomes positively polarized (VII) [9]. In the reaction of alkali with halogenonitrodimedones, the OH^- reacts with the halogen X^+ forming the salt of the corresponding acid HOX (X = Cl, Br, I), With the amines, which also belong to the class of nucleophilic reagents, the bromine and iodine in halogenonitrodimedones evidently react according to the following scheme:

$$RNH_2 + X^+ \longrightarrow [RNH_2X]^+.$$

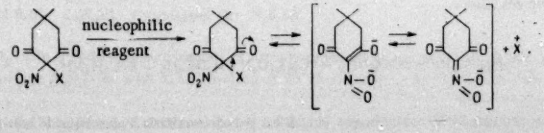
It is possible that the N-halogenoamine cation $(RNH_2X)^+$ forms with the nitrodimedone anion $(C_8H_{10}O_4N)^-$ the intermediate product:

$$[RNH_2X]^+[C_8H_{10}O_4N]^-.$$

It is not possible to isolate a compound of this type in the aromatic series, since it immediately rearranges [10] or is oxidized, but such compounds are known in the aliphatic series [11]. The halogen atom enters the nucleus and the corresponding halogenated aromatic amine, for example bromoaniline, is formed.

Nitroanilines and aminobenzoic acids evidently do not produce a sufficient conjugation effect or else these weak bases are not sufficiently nucleophilic. Phenols similarly do not react with halogenonitrodimedones, while dilute sulfuric acid even stabilizes the halogen atom, so that the halogen atom is split off more readily in water than in dilute acid.

L. Flatow [12] tries to explain the different properties of the 2-halogenoindandiones-1,3 by the existence of two isomeric forms, but this is rejected by G. Vanag and coworkers from a study of the other chemical properties of these substances [13] and also from spectroscopic studies [14]. To explain these phenomena in the 1,3 indandione and dimedone series, the varying electronegativity of the different halogens must obviously be taken into account. Since the chlorine atom is the most electronegative (3.0 eV) [15] it forms a positively charged ion only in the presence of strong alkalies, whereas with iodine (2.5 eV) and bromine (2.8 eV) this takes place even in the presence of aromatic amines:



This reaction is reversible and so the presence of a positive halogen ion is necessary for the preparation of halogenonitrodimedones. Thus, for example, nitrodimedone in glacial acetic acid shows practically no reaction with chlorine or bromine, but on the addition of water the corresponding halogenonitrodimedone is formed immediately. The water and the halogen form HOX, which may give positive halogen ion on dissociation.

EXPERIMENTAL

The dioxane-iodine monochloride complex. 6 g iodine, 70 ml carbon tetrachloride, 3.2 g (2 ml) sulfuryl chloride and .4 g anhydrous aluminum chloride were heated under a reflux fitted with a calcium chloride tube for 5 minutes. The reflux condenser was then replaced by an ordinary condenser and the iodine monochloride and

solvent distilled off on a water bath. 2 g (2 ml) dioxane was added to the distillate obtained. The reaction mixture became warm and orange needle-like crystals were precipitated. These were separated and washed with carbon tetrachloride. Yield 5.5 g (56%) of complex. M.p. 103° (with decomp.). The chlorine was determined, after removal of the iodine, by the Volhard method.

Found %: Cl 17.39. $C_4H_8O_2 \cdot 2I$ Cl. Calculated %: Cl 17.19

4-Nitro-4-iodo-1,1-dimethylcyclohexanedione-1,3 (Iodonitrodimedone, II, X = I)

a) 1 g of finely-ground iododimedone and 1 ml of a mixture prepared from 2 ml of glacial acetic acid and 0.5 ml of fuming nitric acid (d 1.51) were added with stirring to 5 ml of glacial acetic acid. The mixture became warm, the iododimedone dissolved and yellow crystals of iodonitrodimedone began to precipitate. Yield 0.51 g (45%). M. p. 144° (with decomp.).

b) 50 ml of water was added to a solution of 1.85 g nitrodimedone and 2.07 g of the dioxane-iodine monochloride complex prepared above in 5 ml glacial acetic acid. A pale yellow precipitate of iodonitrodimedone was obtained. Yield 2.76 g (92%). M. p. 146° (with decomp.).

Found %: N 4.31. $C_8H_{10}O_4NI$. Calculated %: N 4.50.

Decomposition of chloronitrodimedone with alkali. 0.8 g chloronitrodimedone was shaken up with 10 ml 0.1 N caustic soda. After 5 minutes all the chloronitrodimedone had dissolved with the formation of a deep red solution. A sharp odor of chlorinated nitromethane was produced. On acidification an orange oil separated and was extracted with benzene. After removal of the benzene an orange substance remained which crystallized in the form of long needles on prolonged standing in a desiccator. M.p. 55-60°. The substance was readily soluble in water. A slight precipitate appeared when bromine was added to this solution. This was recrystallized from carbon tetrachloride and pure bromonitrodimedone obtained. M.p. 140°. A mixture with known bromonitrodimedone gave no melting point depression.

3-4 ml of concentrated hydrochloric acid was added to the solution remaining after the extraction with benzene. A very slight precipitate was obtained. After crystallization from benzene pure β,β-dimethylglutaric acid was obtained. Needles with m.p. 103°.

The Reaction of Bromonitrodimedone with Aromatic Amines

Aniline. 1.4 g aniline was added to a solution of 2 g bromonitrodimedone in 15 ml benzene (molar ratio of reactants 2:1). A precipitate formed rapidly – the aniline salt of nitrodimedone. M.p. 150° [1]. Yield 2 g (95%) according to the reaction:

$$C_8H_{10}O_4NBr + 2C_6H_5NH_2 \rightarrow C_8H_{11}O_4N \cdot H_2NC_6H_5 + BrC_6H_4NH_2.$$

The filtrate was saturated with dry hydrogen chloride. p-Bromoaniline hydrochloride was precipitated. Yield 1 g (40%).

Found %: N 6.71. C_6H_6NBr. HCl. Calculated %: N 6.71.

With acetyl chloride, 4-bromoacetanilide was obtained. M.p. 162° (according to the literature data 165°).

Found %: N 6.78. C_8H_8ONBr. Calculated %: N 6.54.

p-Toluidine. The p-toluidine salt of nitrodimedone was obtained in 96% yield by a reaction analogous to that of aniline. M.p. 161° [1]. The filtrate was evaporated to dryness and treated with acetyl chloride.

Melting point of o-bromo-p-acetotoluide after recrystallization from dilute alcohol 117° (according to the literature data 118°).

Found %: N 6.29. $C_9H_{10}ONBr$. Calculated %: N 6.14.

m-Toluidine. With a molar ratio of the reactants of 1:1 the p-bromo-m-toluidine salt of nitrodimedone was precipitated in 64% yield. M.p. 144°. The salt was treated with alkali and the p-bromo -m-toluidine which separated was recrystallized from dilute alcohol. M.p. 81-82° (according to the literature data 81°).

Found %: N 7.82. C_7H_8NBr. Calculated %: N 7.53.

o-Toluidine. The salt precipitated very slowly. The benzene filtrate was evaporated to dryness and treated with benzoyl chloride. After crystallization from dilute alcohol bromo-o-benzotoluide with m.p. 155° was obtained.

Found %: N 5.14. $C_{14}H_{12}NOBr$. Calculated %: N 4.83.

α-Naphthylamine. By a reaction similar to that of m-toluidine the 4-bromo-α-naphthylamine salt of nitrodimedone was precipitated in 60% yield. M.p. 144° (with decomp.).

Found %: N 6.54. $C_{18}H_{19}O_4N_3Br$. Calculated %: N 6.85.

After treatment with alkali and recrystallization from dilute alcohol pure 4-bromo- α-naphthylamine with m.p. 100° was obtained (according to the literature data 102°).

β-Naphthylamine. By a reaction similar to that of aniline the β-naphthylamine salt of nitrodimedone was precipitated in 100% yield. The benzene filtrate was evaporated and acetylated. After recrystallization from aqueous alcohol the α-bromo-β-naphthylacetamide melted at 137° (according to the literature data 140°).

Found %: N 5.03. $C_{12}H_{10}NOBr$. Calculated %: N 5.30.

The Reaction of Iodonitrodimedone with Aromatic Amines

Benzene solutions of iodonitrodimedone and the aromatic amine (1:1) were mixed.

Aniline. The p-iodoaniline salt of nitrodimedone was precipitated. Yield 69%. M.p. 135°. p-Iodoaniline was separated with alkali and melted at 66° (according to the literature data 67°).

Found %: N 6.09. C_6H_6NI. Calculated %: N 6.38.

o-Toluidine. The p-iodo-o-toluidine salt of nitrodimedone was precipitated. Yield 52%. M. P. 118-120°. The p-iodo-o-toluidine separated with alkali melted at 85° (according to the literature data 87°).

Found %: N 6.17. C_7H_8NI. Calculated %: N 6.01.

m-Toluidine. The p-iodo-m-toluidine salt of nitrodimedone was precipitated. Yield 69%. M.p. 143°. The p-iodo-m-toluidine separated with alkali was benzoylated. The benzoyl derivative melted at 127°.

Found %: N 4.49. $C_{14}H_{12}ONI$. Calculated %: N 4.15.

p-Toluidine. With double the amount of p- toluidine, the p-toluidine salt of nitrodimedone was precipitated. Yield 80%. The filtrate was evaporated and benzoylated. The o-iodo-p-benzotoluide after recrystallization from dilute alcohol had m.p. 157° (according to the literature data 161°).

Found %: N 4.03. $C_{14}H_{12}ONI$. Calculated %: N 4.15.

The Reaction of Chloronitrodimedone with Aromatic Amines

Aniline. 0.34 g aniline was added to a solution of 0.80 g chloronitrodimedone in 10 ml benzene and evaporated to dryness after 12 hours. The residue was treated with concentrated ammonia solution and filtered. 0.32 g (35%) of N-nitrodimedonylaniline or 2-anilino-2-nitrodimedone (V, R = C_6H_5) remained on the filter. Yellow needles with m.p. 154° after crystallization from aqueous alcohol. The substance dissolved readily in alcohol, ether, chloroform, and glacial acetic acid, did not dissolve in water.

Found %: N 10.28. $C_{14}H_{16}O_4N_2$. Calculated %: N 10.14.

p-Toluidine. 0.39 g p-toluidine and 0.80 g chloronitrodimedone in 5 ml glacial acetic acid were heated for a short time to 60-70°, then diluted with water and treated with ether. The ether extract was evaporated and the residue treated with concentrated ammonia solution. The insoluble residue was recrystallized from aqueous alcohol and fine light brown crystals of N-nitrodimedonyl-p-toluidine or 2-p-toluidino-2-nitrodimedone were obtained. M.p. 188°.

Found %: N 9.68. $C_{15}H_{18}O_4N_2$. Calculated %: N 9.66.

SUMMARY

1. A new complex of iodine monochloride and dioxane $C_4H_8O_{21} \cdot 2ICl$ and 2-iodo-2-nitrodimedone have been prepared.

2. It has been shown that in alkaline solutions the halogenonitrodimedones split off HOX (X=Cl, Br, I), while partial decomposition and oxidation of the nitrodimedone takes place.

3. It has been shown that iodo-and bromonitrodimedones halogenate the aromatic amines studied. Chloronitrodimedone gives N-nitrodimedonylamines (2-arylamino-2-nitrodimedones).

4. The halogen in the halogenonitrodimedones is positively polarized in reactions with nucleophilic reagents as a result of the conjugation of σ-and π-bonds.

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INDOLE DERIVATIVES

I. THE SYNTHESIS OF N-BENZYL-1,2,3,4-TETRAHYDROCARBAZOLES

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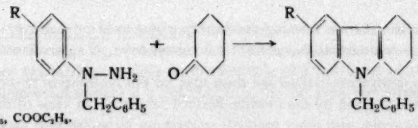
N-Benzyl-1,2,3,4-tetrahydrocarbazoles, which are of interest in the synthesis of certain physiologically active substances, have not been studied up to the present. Since the most suitable method for preparing them was difficult to choose on the basis of the literature data, we undertook a comparative study of three possible routes to their synthesis.

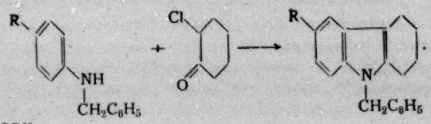
The basis of the first method was the Fischer–Borsche reaction [1] – the reaction of arylhydrazines and cyclohexanone. While the condensation of monosubstituted hydrazines with cyclohexanone has been well studied, the reaction of unsymmetrical condensation disubstituted hydrazines, leading to the formation of N-substituted tetrahydrocarbazoles, has hardly been studied at all. We carried out a number of examples of this reaction by condensations with N-phenyl-N-benzylhydrazines containing substituents in the aromatic nucleus:



R=H, CH_3, OC_2H_5, $COOC_2H_5$.

The reaction was carried out by heating equimolecular amounts of arylbenzylhydrazine and cyclohexanone, after which the hydrazone obtained was subjected, without separation, to cyclization with dilute sulfuric acid. After the usual treatment the corresponding tetrahydrocarbazoles were obtained in 75-85% yield. Although the reaction itself gives excellent results, the synthesis of the original N,N-disubstituted hydrazines presents well-known preparative difficulties. The most suitable method for their preparation proved to involve the nitrosation of N-monosubstituted aromatic amines with subsequent reduction of the nitrosamines with zinc dust in a mixture of alcohol and acetic acid. In this way we obtained, in fairly good yield, N-phenyl-N-benzylhydrazine, N-p-tolyl-N-benzylhydrazine, N-p-ethoxyphenyl-N-benzylhydrazine, and N-p-carbethoxyphenyl-N-benzylhydrazine.

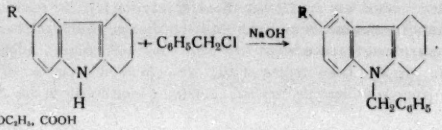
In order to avoid the fairly troublesome synthesis of the disubstituted hydrazines, we studied the possibility of preparing 1,2,3,4-tetrahydrocarbazoles by the condensation of substituted N-benzylanilines with 2-chlorocyclohexanone. The synthesis of carbazoles by the reaction of primary aromatic amines with chlorocyclohexanone, leading to tetrahydrocarbazoles without substituents on the nitrogen atom, has been described in the literature [2]. The possibility of synthesizing N-substituted tetrahydrocarbazoles in this way has only been indicated in the patent literature [3], where it is stated that the synthesis gives almost quantitative yields, but the reaction conditions are not given. The condensation of 2-chlorocyclohexanone and secondary amines carried out by us gave positive results, but the yields of N-substituted 1,2,3,4-tetrahydrocarbazoles were relatively low.



R=H, Cl, CH_3, OC_2H_5.

The reaction was carried out by heating chlorocyclohexanone with double the quantity of aromatic amine, the excess of which combined with the hydrogen chloride formed. The yields of N-benzyl-1,2,3,4-tetrahydrocarbazoles were 25-40%: N-methyl-1,2,3,4-tetrahydrocarbazole was obtained in this way in higher yield (60%). In spite of the relatively low yields, this method has its advantages in its simplicity and in the greater availability of the starting materials.

A third route to the synthesis of N-substituted tetrahydrocarbazoles is provided by the direct benzylation of tetrahydrocarbazoles with an unsubstituted nitrogen atom. We carried out this synthesis by the reaction of 1,2,3,4-tetrahydrocarbazoles with benzyl chloride in a concentrated solution of alkali in aqueous acetone [4]. With compounds containing no reactive groups, the yields of the N-benzyl derivatives reached 50-60%. On the other hand, 6-carbethoxy-1,2,3,4-tetrahydrocarbazole was benzylated in only 23% yield.



R=H, Cl, $COOC_2H_5$, COOH

It is interesting to note, that on treating the corresponding acid – 6-carboxy-1,2,3,4-tetrahydrocarbazole – in the same way, the N-benzyl derivative, and not the benzyl ester, is again formed.

The results of the experiments carried out show that for the synthesis of N-benzyl-1,2,3,4-tetrahydrocarbazoles the best results are given by the Fischer-Borsche reaction. In view of the greater availability of their starting materials, however, two other methods worked out by us are also useful - direct benzylation and the condensation of secondary amines with chlorocyclohexanone. These last two methods are particularly convenient in those cases where the synthesis of tetrahydrocarbazole derivatives of relatively simple structure is being considered.

EXPERIMENTAL

I. The Synthesis of Disubstituted Hydrazines

N,N-Benzyl-p-ethoxyphenylhydrazine. N-Benzyl-p-phenetidine was obtained by a reaction analogous to the synthesis of benzylaniline [5] from 450 g p-phenetidine, 102 g benzyl chloride and 90 g sodium bicarbonate in 90 ml water. Yield 136 g (79.5%, calculated from benzyl chloride), b.p. 176-180° (3-4 mm).

Nitrosation was carried out by analogy with the preparation of benzylphenylnitrosamine [6]. 21.5 g (94%) of nitroso-compound with m.p. 49-51° was obtained from 20 g N-benzyl-p-phenetidine, 12 g sodium nitrite and 18 ml of sulfuric acid in a mixture of 33 ml water and 250 ml alcohol.

20-30 ml of acetic acid was gradually added with stirring to a solution of 21.5 g of the nitrosamine in 150 ml alcohol and 25 g zinc dust. The residue was filtered off, the alcohol distilled off under vacuum at the water pump, the residue poured into water, made alkaline and extracted with ether. The ether extract was shaken up with concentrated hydrochloric acid, and the crystals of N-benzyl-N-p-ethoxyphenylhydrazine hydrochloride which precipitated were filtered off. Yield 12 g (51.2%), m.p. 151-153°.

N-Benzyl-N-p-carbethoxyphenylhydrazine. The synthesis was carried out similarly to that described above. 400 g ethyl p-aminobenzoate and 70 g benzyl chloride gave 130 g (92%) of ethyl N-benzyl-p-aminobenzoate, b.p. 216-217° (2 mm). 45 g (81%) of the nitrosamine with m.p. 74-76° was obtained from 50 g of this substance. On reduction of the nitrosamine by the method described above 14 g (66%) of N-benzyl-N-p-carbethoxyphenylhydrazine hydrochloride with m.p. 182-185° was obtained.

II. The Synthesis of N-benzyl-1,2,3,4-Tetrahydrocarbazoles from Disubstituted Hydrazines

9-Benzyl-1,2,3,4-tetrahydrocarbazole. A mixture of 1 g N-benzyl-N-phenylhydrazine hydrochloride and 0.5 g cyclohexanone was heated gently on a water bath until a vigorous reaction, accompanied by great evolution of heat, began. At the end of the reaction the mixture was heated for a further 30 minutes on a water bath. 10 ml of dilute sulfuric acid (1:10) was added to the hot solution and heating continued for a further 30 minutes. The colorless oil which formed was separated from the water and after standing for a week at room temperature it gradually crystallized. Yield of 9-benzyl-1,2,3,4-tetrahydrocarbazole 1.2 g (90%), m.p. 46-48°. Recrystallization from alcohol gave 0.8 g colorless plates, m.p. 50-51°.

Found %: N 5.22, 5.23. $C_{19}H_{19}N$. Calculated %: N 5.36.

The substance dissolved readily in ether, benzene and chloroform, with difficulty in methanol, sparingly in petroleum ether.

6-Methyl-9-benzyl-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 1.5 g N-benzyl-N-p-tolylhydrazine hydrochloride and 0.6 g cyclohexanone. After similar treatment 1.2 g (75%) of material was obtained, which after recrystallization from a mixture of alcohol and ethyl acetate (1:1) had m.p. 99.5-100.5°.

Found %: N 5.02, 5.05. $C_{20}H_{21}N$. Calculated %: N 5.08.

6-Ethoxy-9-benzyl-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 2 g N-benzyl-N-p-ethoxyphenylhydrazine hydrochloride and 1 g cyclohexanone. The colorless oil obtained from this reaction and the similar subsequent treatment crystallized rapidly on the addition of a few drops of alcohol. Yield of 6-ethoxy-9-benzyl-1,2,3,4-tetrahydrocarbazole 1.8 g (85.6%), m.p. 78-79° after recrystallization from alcohol.

Found %: N 4.58, 4.62. $C_{21}H_{23}ON$. Calculated %: N 4.56.

The substance dissolved readily in ether, benzene, acetone and chloroform, with difficulty in alcohol, methanol, petroleum ether.

6-Carbethoxy-9-benzyl-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 5 g N-benzyl-N-p-carbethoxyphenylhydrazine hydrochloride and 1.6 g cyclohexanone. After the treatment described 4.6 g of material (85%) was isolated, which after recrystallization from alcohol had m.p. 108-109°.

Found %: N 4.49, 4.42. $C_{22}H_{23}O_2N$. Calculated %: N 4.58.

2.5 g of 6-carbethoxy-9-benzyl-1,2,3,4-tetrahydrocarbazole was boiled for 1 hour with 30 ml of a 7% alcohol solution of caustic soda, after which the solution was neutralized with an alcoholic solution of hydrogen chloride. The crystals which precipitated were filtered off and washed with water. The yield of 6-carboxy-9-benzyl-1,2,3,4-tetrahydrocarbazole was 2.25 g (90%). On recrystallization from alcohol it formed fine light yellow needles with m.p. 234-236°.

Found %: N 4.46, 4.47. $C_{20}H_{19}O_2N$. Calculated %: N 4.58.

III. The Synthesis of N-benzyl-1,2,3,4-Tetrahydrocarbazoles from Secondary Amines

9-Methyl-1,2,3,4-tetrahydrocarbazole. 3.3 g N-methylaniline and 2 g 2-chlorocyclohexanone were heated at 150-160° for 1.5 hours, 20 ml water and 5 ml concentrated hydrochloric acid were added, the mixture heated to boiling, cooled and extracted three times with ether, The extracts were washed with dilute hydrochloric acid, sodium carbonate solution and water, dried over sodium sulfate and the ether distilled off. 1.8 g (66%) of 9-methyl-1,2,3,4-tetrahydrocarbazole was obtained, which after recrystallization from methanol had m.p. 49-50°.

Literature data [7]: m.p. 50°.

9-Benzyl-1,2,3,4-tetrahydrocarbazole. This was prepared similarly from 13.6 g N-benzylaniline and 5 g chlorocyclohexanone. After similar treatment 4.3 g (43%) of 9-benzyl-1,2,3,4-tetrahydrocarbazole was obtained as an almost colorless oil with b.p. 207-211° (5 mm).

Found %: N 5.73, 5.58. $C_{19}H_{19}N$. Calculated %: N 5.36

The material obtained did not crystallize even after several distillations, unlike the specimen prepared by the Fischer–Borsche reaction. It evidently contained some impurity in such small amount that it was not even shown in the analysis results. The yield of 9-benzyl-1,2,3,4-tetrahydrocarbazole was not increased when the reaction was carried out in boiling xylene.

9-Benzyl-6-methyl-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 6 g N-benzyl-p-toluidine and 2 g chlorocyclohexanone. Yield 1.3 g (32%). Colorless needles with m.p. 99.5-100.5° after recrystallization from a mixture of alcohol and ethyl acetate. A mixture with the sample obtained from the hydrazine (see above) did not give a melting point depression.

9-Benzyl-6-chloro-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 6.6 g N-benzyl-p-chloroaniline and 2 g chlorocyclohexanone. After similar treatment 1.2 g (26.5%) 9-benzyl-6-chloro-1,2,3,4-tetrahydrocarbazole was obtained, which crystallized from alcohol as colorless needles with m.p. 97.5-98.5°.

Found %: N 4.77, 4.78; Cl 11.46, 11.62. $C_{19}H_{18}NCl$. Calculated %: N 4.75; Cl 11.97

The material dissolved in benzene and acetone, with difficulty in alcohol.

9-Benzyl-6-ethoxy-1,2,3,4-tetrahydrocarbazole. 2 g chlorocyclohexanone was added slowly and with vigorous stirring to 6.8 g N-benzyl-p-phenetidine previously heated to 140-150°, after which the mixture was heated for a further 30 minutes at the same temperature. After the treatment described above, 2.1 g (39%) of 9-benzyl-6-ethoxy-1,2,3,4-tetrahydrocarbazole was obtained, which had m.p. 78-79° after recrystallization from alcohol. A mixture with the specimen prepared from the hydrazine (see above) gave no melting point depression.

IV. Benzylation of Tetrahydrocarbazoles

9-Benzyl-1,2,3,4-tetrahydrocarbazole. A mixture of 10 g 1,2,3,4-tetrahydrocarbazole, 9 g benzyl chloride, 15 ml 60% aqueous caustic potash solution and 60 ml acetone was heated with stirring on a water bath for 2 hours. The reaction mass was poured into water, extracted twice with benzene or ether, the extracts dried over sodium sulfate, the benzene and excess benzyl chloride distilled off and the residue distilled in vacuo. 8.6 g of oily material with b.p. 207-211° (5 mm) was obtained; it did not crystallize even on prolonged standing.

9-Benzyl-6-chloro-1,2,3,4-tetrahydrocarbazole. This was obtained similarly, yield 54%. After recrystallization from alcohol the material had m.p. 97.5-98.5°. A mixture with the specimen prepared from the secondary amine (see above) gave no melting point depression.

9-Benzyl-6-carbethoxy-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 4 g 6-carbethoxy-1,2,3,4-tetrahydrocarbazole, 2.5 g benzyl chloride and 8 ml 60% aqueous caustic potash solution in 30 ml acetone. Yield 1.3 g (23%). Colorless crystals with m.p. 108-109° after recrystallization from alcohol. A mixture with the material prepared from the hydrazine (see above) gave no melting point depression.

9-Benzyl-6-carboxy-1,2,3,4-tetrahydrocarbazole. This was obtained similarly from 2 g 6-carboxy-1,2,3,4-tetrahydrocarbazole and 2.5 g benzyl chloride. Yield 0.8 g (28%). Colorless crystals with m.p. 234-236° after recrystallization from acetic acid. A mixture with the specimen prepared by hydrolysis of the 6-carbethoxy derivative (see above) gave no melting point depression.

SUMMARY

1. Threee methods have been worked out for the synthesis of N-benzyl-1,2,3,4-tetrahydrocarbazoles—the condensation of N-benzyl-N-arylhydrazines with cyclohexanone, the condensation of N-benzylanilines with 2-chlorocyclohexanone and the reaction of benzyl chloride with 1,2,3,4-tetrahydrocarbazoles in the presence of alkali.

2. It has been shown that the highest yields of N-benzyl-1,2,3,4-tetrahydrocarbazoles are obtained by using the first of the methods listed.

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INDOLE DERIVATIVES

II. THE SYNTHESIS OF SOME DERIVATIVES OF 1,2,3,4-TETRAHYDRO-γ-CARBOLINE

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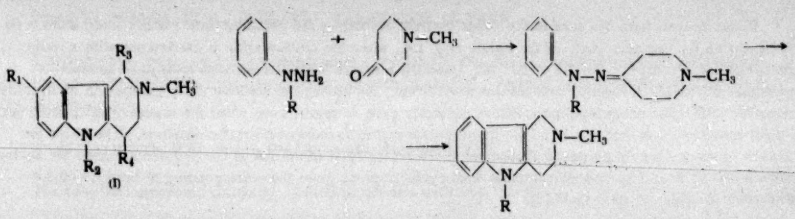
The literature at the present time contains a considerable amount of data on the pharmacological activity of β-carboline derivatives [1]. The isomeric γ-carbolines have not been studied very much, however, and a report of their high antihistamine activity has only appeared recently [2]. It appeared of interest to us to synthesize a series of derivatives of 1,2,3,4-tetrahydro-γ-carboline of type (I), with different substitutents in the aromatic and carboline nuclei, for extended pharmacological tests. To achieve the synthesis of such compounds we used the Fischer reaction, which was first employed for the preparation of these compounds by Cook and Reed [3]. This reaction is based on the cyclization of the phenylhydrazones of the corresponding γ-piperidones under the influence of acidic reagents (zinc chloride, dilute sulfuric acid, acetic acid, phosphoric acid, bromine trifluoride, etc.) and takes place according to the scheme:

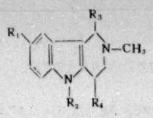


In spite of the large number of works on the use of the Fischer reaction for the preparation of different indole derivatives, a method for synthesizing tetrahydro-γ-carbolines based on the condensation described above cannot be said to have been sufficiently well worked out. It is usually necessary to choose the experimental conditions for each particular case in order to obtain acceptable results.

We also encountered considerable difficulties in achieving a synthesis of the tetrahydro-γ-carboline derivatives in which we were interested, and therefore made a more detailed study of the cyclization conditions for arylhydrazones of γ-piperidones, which depend on their structure. It turned out that the condensation of N-methylpiperidone itself takes place under the conditions described earlier [2], i.e., by heating it directly with the arylhydrazines in the presence of dilute sulfuric acid, as we have shown, for example, by the synthesis of 3,6-dimethyl-9-benzyl-1,2,3,4-tetrahydro-γ-carboline. The yields using this method, however, were low. At the same time the cyclization of the arylhydrazones of 1,3-dimethyl- and 1,2,5-trimethylpiperidones leads to the formation of an extremely tarry reaction mixture, and individual compounds cannot in general be separated. The use of zinc chloride, phosphoric or polyphosphoric acids or acetic acid as cyclizing agents did not give the desired results. The cyclization was successfully achieved only by the use of a 7-10% hydrogen chloride solution as condensing agent [4]. In all the cases studied by us this method gave better results than the cyclization with sulfuric acid described above and may be considered a more convenient and universal method for the synthesis of tetrahydro-γ-carbolines. In some cases it is more convenient to carry out the reaction with arylhydrazones which have been isolated in the pure state; these can be prepared in good yields by the

direct action in water of 1,3-dimethyl- and 1,2,5-trimethylpiperidone hydrochlorides with the corresponding arylhydrazines. Using this method we have prepared a series of substituted 1,2,3,4-tetrahydro-γ-carbolines, whose synthesis data are given in the Table.

TABLE Synthesis of 1,2,3,4-Tetrahydro-γ-carbolines



R_1	R_2	R_3	R_4	Yield (%)	Melting point of the base	Melting point of the HCl
OC_2H_5	H	H	H	62.0	97—98°	214—216°
H	H	H	CH_3	78.0	—	189—190
OC_2H_5	H	H	CH_3	23.0	79—80	177—179
H	H	CH_3	CH_3	86.0	—	181—183
OC_2H_5	H	CH_3	CH_3	48.0	70—71	162—163
CH_3	$CH_2C_6H_5$	H	H	31.0	97—98	255—256
OC_2H_5	$CH_2C_6H_5$	H	H	16.0	88—89	247—249
H	$CH_2C_6H_5$	H	CH_3	11.0	—	214—216

It can be seen from the data in the Table that the carbolines are obtained most readily when there is no substituent on the nitrogen atom of the indole ring, i.e., when the condensation is carried out with a monosubstituted arylhydrazine. On the other hand, when the reaction is carried out with N-aryl-N-benzylhydrazines the yields of reaction product are much lower. An attempt to achieve the condensation of disubstituted hydrazines with 1,2,5-trimethylpiperidones-4 generally gave no result, even when the reaction was carried out in mild conditions; in this case even the intermediate arylhydrazones could not be obtained. The reason for this lack of success should be sought first of all in the difficulty of formation of the hydrazone, since the analogous condensation of N-aryl-N-benzylhydrazines with cyclohexanone gives the corresponding N-benzyl-1,2,3,4-tetrahydrocarbazoles in good yield [5].

The tetrahydro-γ-carbolines obtained are crystalline, fairly stable substances which form hydrochlorides readily. A well-known pharmacological interest is also attached to the alkyl carbolinium halides, in connection with which we carried out the synthesis of two methyl carbolinium iodides, which are readily obtained by the reaction of the base carboline with methyl iodide.

All the compounds prepared were tested for their physiological activity.

EXPERIMENTAL

3,6-Dimethyl-9-Benzyl-1,2,3,4-tetrahydro-γ-carboline. 0.5 g N-benzyl-N-p-tolylhydrazine hydrochloride and 0.3 g 1-methylpiperidone-4 hydrochloride in 10 ml dilute sulfuric acid (1:10) were boiled for 45 minutes. The precipitate which formed was filtered off and dried in air (yield 0.5 g). The carboline sulfate obtained was dissolved in water and made alkaline by the addition of 10% aqueous caustic soda solution. The precipitated oil crystallized rapidly, the crystals were filtered off, washed with water and recrystallized from aqueous alcohol (1:1). Yield of 3,6-dimethyl-9-benzyl-1,2,3,4-tetrahydro-γ-carboline 0.3 g (31%); fine colorless needles with m.p. 97-98°.

Found %: N 9.87, 9.94. $C_{20}H_{22}N_2$. Calculated %: N 9.64.

0.15 g of the base was dissolved in ether and dry hydrogen chloride passed into the solution. The precipitated hydrochloride was filtered off, washed with ether and dried. Colorless needles with m.p. 255-257° (decomp.).

Found %: Cl 10.31, 10.35. $C_{20}H_{23}N_2Cl$. Calculated %: Cl 10.84

1,3-Dimethyl-1,2,3,4-tetrahydro-γ-carboline. 1.1 g phenylhydrazine hydrochloride was added to a solution of 1 g 1,3-dimethylpiperidone-4 in 20 ml of a 10% alcohol solution of hydrogen chloride and the reaction mixture heated to boiling for 2 hours, after which it was left for 1 day at room temperature. The precipitate of 1,3-dimethyl-1,2,3,4-tetrahydro-γ-carboline hydrochloride which formed was filtered off. Yield 1.4 g (78%). Fine colorless needles with m.p. 189-190° (decomp.) after crystallization from absolute alcohol.

Found %: N 12.11, 12.19. $C_{13}H_{17}N_2Cl$. Calculated %: N 11.83

3-Methyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carboline. Obtained similarly from 2 g 1-methylpiperidone-4 and 2 g p-ethoxyphenylhydrazine in 35 ml of 10% hydrogen chloride solution in alcohol. Yield of hydrochloride 2.9 g (62%), m.p. 214-216° (decomp.).

Found %: N 10.35, 10.25; Cl 13.21, 13.18. $C_{14}H_{19}ON_2Cl$. Calculated %: N 10.50; Cl 13.24.

The hydrochloride was dissolved in water and 10% aqueous caustic soda solution added; the oil which precipitated crystallized rapidly. The base 3-methyl-6-ethoxy-1,2,3,4-tetrahydrocarboline – colorless needles with m.p. 151-152°.

Found %: N 11.94, 12.01. $C_{14}H_{18}ON_2$. Calculated %: N 12.16

1,3-Dimethyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carboline. Obtained similarly from 2 g 1,3-dimethylpiperidone-4 in 30 ml of 10% hydrogen chloride solution in alcohol. Yield of hydrochloride 1 g (23%), m.p. 177-179° (decomp.).

Found %: N 9.69, 9.67. $C_{15}H_{21}ON_2Cl$. Calculated %: N 9.97.

The base was separated similarly. Colorless needles with m.p. 79-80°.

Found %: N 11.25, 11.17. $C_{15}H_{20}ON_2$ Calculated %: N 11.47

3-Methyl-6-ethoxy-9-benzyl-1,2,3,4-tetrahydro-γ-carboline. Obtained similarly from 2 g 1-methylpiperidone-4 and 3.7 g N-benzyl-N-p-ethoxy-phenylhydrazine [5] in 40 ml 7% hydrogen chloride solution in alcohol. The reaction mixture was heated for 1 hour and left for 1 day at room temperature. After the treatment described above 1.3 g (23%) of hydrochloride with m.p. 247-249° (decomp.). was obtained.

Found %: N 7.77, 7.72; Cl 9.95, 9.92. $C_{21}H_{25}ON_2Cl$. Calculated %: N 7.85; Cl 9.93.

The base was separated similarly. Colorless needles with m.p. 88-89° (from 1:1 aqueous alcohol).

Found %: N 8.52, 8.45. $C_{21}H_{24}ON_2$. Calculated %: N 8.74.

1,3-Dimethyl-9-benzyl-1,2,3,4-tetrahydro-γ-carboline. Obtained from 2 g 1,3-dimethylpiperidone-4 and 3.6 g N-benzyl-N-phenylhydrazine hydrochloride in 30 ml 7% hydrogen chloride solution in alcohol. The reaction mixture was heated to boiling and left for 1 day at room temperature. Yield of hydrochloride 0.6g (11%). Colorless crystals with m.p. 214-216° (from anhydrous alcohol).

Found %: N 8.32, 8.28; Cl 10.90, 10.90. $C_{20}H_{23}N_2Cl$. Calculated %: N 8.56; Cl 10.84.

1,3,4-Trimethyl-1,2,3,4-tetrahydro-γ-carboline. 4 g 1,2,5-trimethylpiperidone-4 was added to a solution of 4 g phenylhydrazine hydrochloride in 25 ml water. The reaction mixture became warm and after 30 minutes a copious precipitate of the hydrazone was formed. Filtered off and washed with water. Yield of 1,2,5-trimethylpiperidone-4 phenylhydrazone hydrochloride 6 g. Colorless crystals with m.p. 207-209° after recrystallization from alcohol.

Found %: N 15.89, 15.81. $C_{14}H_{22}N_3Cl$. Calculated %: N 15.69.

3.3 g of the phenylhydrazone hydrochloride obtained was added to 30 ml of 7% hydrogen chloride solution in alcohol and the reaction mixture carefully heated until the spontaneous evolution of heat began and the solution boiled. The phenylhydrazone precipitate dissolved and shortly afterwards 1,3,4-trimethyl-1,2,3,4-tetrahydro-γ-carboline hydrochloride began to crystallize out. After the usual treatment 2.7 g of material was obtained (86%, calculated from the original piperidone). Crystals with m.p. 181-183° (decomp.), were obtained after recrystallization from alcohol.

Found %: N 11.20, 11.05; Cl 14.02, 13.90. $C_{14}H_{19}N_2Cl$. Calculated %: N 11.17; Cl 14.13.

1,3,4-Trimethyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carboline. 1,2,5-piperidone-4-p-ethoxyphenylhydrazone hydrochloride was obtained similarly (as above) from 1.2 g p-ethoxyphenylhydrazine hydrochloride and 0.8 g 1,2,5-trimethylpiperidone in 10 ml water. Yield 1.1 g, m. p. 168-170° (decomp.) after recrystallization from water.

Found %: N 13.49, 13.45. $C_{16}H_{26}ON_3Cl$. Calculated %: N 13.47.

0.7 g (48%) 1,2,4-trimethyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carboline hydrochloride was obtained from 1.5 g of the above material by the method described in the previous example (20 ml 7% hydrogen chloride solution), m.p. 162-163°.

Found %: N 9.22, 9.30; Cl 11.70, 11.79. $C_{16}H_{23}ON_2Cl$. Calculated %: N 9.50; Cl 12.02.

The base was isolated from the hydrochloride obtained in the usual way. Colorless needles with m.p. 70-71° after recrystallization from aqueous alcohol (1:1).

Found %: N 10.55, 10.74. $C_{16}H_{22}ON_2$. Calculated %: N 10.84.

1,3,3-trimethyl-1,2,3,4-tetrahydro-γ-carbolinium iodide. 0.5 g 1,3-dimethyl-1,2,3,4-tetrahydro-γ-carboline hydrochloride was dissolved in water, 10% caustic soda solution added, the oil which precipitated was extracted with ether, the extract was dried over sodium sulfate, poured from the drying agent and 0.25 g methyl iodide added. The precipitate which formed after 1 day was filtered off and washed with ether. Yield 0.6 g (83%). Fine needles with m.p. 218-220° after recrystallization from water.

Found %: N 8.44, 8.56; I 37.09, 37.11. $C_{14}H_{19}N_2I$. Calculated %: N 8.18; I 37.08.

1,3,3,4-Tetramethyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carbolinium iodide. 0.15 g 1,3,4-trimethyl-6-ethoxy-1,2,3,4-tetrahydro-γ-carboline and 0.15 g methyl iodide in 8 ml ether were set aside to stand for 1 day. After the usual treatment the yield of the quaternary methyl iodide was 0.2 g (87%). Fine crystals with m.p. 207-208° after recrystallization from water.

Found %: N 6.94, 6.81; I 31.78, 31.67. $C_{17}H_{25}ON_2I$. Calculated %: N 6.99; I 31.70.

SUMMARY

1. It has been shown that an alcoholic solution of hydrogen chloride is a convenient condensing agent for the preparation of 1,2,3,4-tetrahydro-γ-carboline derivatives from the corresponding arylhydrazones of substituted γ-piperidones.

2. Several representatives of the 1,2,3,4-tetrahydro-γ-carboline series have been prepared by this method.

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* T. p. = C. B. Translation pagination.

THE CHEMISTRY OF SELENOPHEN

IV. THE IODINATION AND METALLATION OF SELENOPHEN AND ITS HOMOLOGS. SELENOPHEN CARBOXYLIC ACIDS

Yu. K. Yuryev and N. K. Sadovaya

In connection with studies undertaken by us in the field of selenophen chemistry [1,2,] it became of interest to examine the reaction properties of halogenoselenophens with a view of using these halogen derivatives for the preparation of different types of compounds in the selenophen series.

In a paper by Umesawa [3], who has made the most detailed study of certain reactions of the selenophen ring, it is pointed out that in the conditions of the Grignard reaction all the 2-halogenoselenophens, including 2-iodoselenophen, show hardly any reaction with magnesium, in contrast to the corresponding halogen compounds of the thiophen series. The impossibility of obtaining organomagnesium compounds of the selenophen series led us to turn our attention to the metallation of selenophen by one of the methods used in the thiophen series.

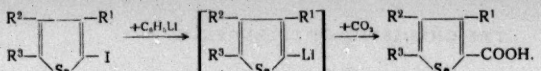
The metallation of thiophen and its homologs, and also of the halogen derivatives of the thiophen series, has been carried out by several methods. Thus thiophen is metallated by sodium amalgam in the presence of alkyl or aryl halide, while 2-chlorothiophen, at temperatures above 50°, is converted to 2-thienylsodium in 84% yield; the metallation of 2-chlorothiophen in ether solution at 30-40° and subsequent carbonation lead to 5-chloro-2-thiophen carboxylic acid in 92% yield, i. e., under these conditions the sodium replaces not the halogen, but the hydrogen in the 5-position of the thiophen nucleus [4]. On metallation of 3-methylthiophen and carbonation of the sodium derivative formed, 3-methyl-5-thiophencarboxylic acid is obtained, i. e., the introduction of the second substituent – the metal – does not take place as usual in the 2-position (halogenation, nitration reactions), but in the 5-position [5]. On metallation of the thiophen nucleus by the action of phenyllithium, 2-thiophencarboxylic acid was obtained from 2-iodothiophen in 58% yield [6].

In 1954 Burlant and Gould metallated dibenzoselenophen by the action of butyllithium and on subsequent carbonation obtained dibenzoselenophen-4-carboxylic acid; by the reaction of dimethyl sulfate, 4-methyldibenzoselenophen was obtained [7].

In the present work a study has been made of the metallation of selenophen and its homologs by the action of phenyllithium on 2-iodoselenophens, which are easily prepared by a method given by us analogous to the preparation of 2-iodothiophen [8]. Assuming that the iodination of 3-methylthiophen and 3-methylselenophen, and also of 2,4-dimethylthiophen and 2,4-dimethylselenophen should take place in exactly analogous fashion, we may take it that on the iodination of 3-methylselenophen in the normal way 2-iodo-3-methylselenophen is obtained, while on the iodination of 2,4-dimethylselenophen, 5-iodo-2,4-dimethylselenophen is obtained. The lithiumselenophens obtained were carbonated and the corresponding carboxylic acids of the selenophen series obtained.

The only acid of the selenophen series which has been described is the selenophen carboxylic acid which was first obtained by Umesawa in 41% yield by the oxidation of 2-propionylselenophen with alkaline permanganate solution [3]. E. G. Kataev and M. V. Palkina obtained the same acid by the oxidation of 2-acetylselenophen. An attempt to prepare selenophen carboxylic and selenophen-2,5-dicarboxylic acids by the permanganate oxidation of 2-methylselenophen and 2,5-dimethylselenophen respectively gave no positive result because of the rupture of the selenophen ring [9].

The method of synthesizing carboxylic acids of the selenophen series described in the present work is quite general and enables the acids to be prepared in fairly good yield. Using this method we prepared the following acids from the corresponding iodides of the selenophen series: selenophen 2-carboxylic acid, 3-methylselenophen-2-carboxylic acid, 2,4-dimethylselenophen-5-carboxylic acid and 3,4-dimethylselenophen-2-carboxylic acid in yields of 50-61%:



(R^1, R^2, R^3=H; R^2, R^3=H, R^1=CH_3; R^2=H, R^1, R^3=CH_3; R_3=H; R^1, R^2=CH_3)

EXPERIMENTAL

I. Iodination of the Selenophen Nucleus

Yellow mercuric oxide and iodine were added alternately in small portions with constant stirring to a solution of selenophen in anhydrous benzene, cooled with ice water. During the reaction, which was accompanied by a slight evolution of heat, the formation of mercuric iodide was observed. The residue was filtered off. The filtrate was washed with sodium thiosulfate solution and water, and dried with calcium chloride. After the solvent had been distilled off, the residue was left to stand over mercuric oxide to remove the iodine which separated and then repeatedly distilled under reduced pressure in a current of nitrogen in the presence of a small quantity of molecular copper. The distillation was accompanied by the partial decomposition of the material and the separation of iodine, as a result of which the iodides obtained were usually of a red color; they readily formed a tarry mass on standing. To purify the specimen from iodine a small quantity of mercuric oxide was added and the mixture left to stand until the red color had disappeared. The pure iodides were liquids of a lemon-yellow color.

2-Iodoselenophen. 6.7 g (52%) of 2-iodoselenophen was obtained from 6.5 g (0.05 mole) selenophen, 12.6 g (0.05 mole) iodine and 8.7 g (0.04 mole) yellow mercuric oxide in 25 ml anhydrous benzene:

B. p. 84–84.5° (11 mm); n_D^{20} 1.6962, d_4^{20} 2.3942, MR_D 41.30; calc. 40.94.
Found %: C 18.55, 18.55; H 1.33, 1.31. C_4H_3ISe. Calculated %: C 18.70; H 1.18.

2-Iodoselenophen is the least stable, on distillation and on standing, of all the iodides of the selenophen series.

2-Iodo-3-methylselenophen. 1.8 g unchanged 3-methylselenophen and 9.6 g (56%, calculated from the 3-methylselenophen which had reacted) of 2-iodo-3-methylselenophen were obtained from 11 g (0.075 mole) 3-methylselenophen, 19 g (0.075 mole) iodine and 14 g (0.06 mole) yellow mercuric oxide in 30 ml anhydrous benzene:

B.p. 93–93.5° (8 mm); n_D^{20} 1.6661, d_4^{20} 2.2522, MR_D 44.73; calc. 45.55.
Found %: C 22.53, 22.49; H 2.04, 2.04. C_5H_5ISe. Calculated %: C 22.16; H 1.86.

5-Iodo-2,4-dimethylselenophen. 0.6 g unchanged 2,4-dimethylselenophen, and 6.4 g (60%, calculated from the 2,4-dimethylselenophen which had reacted) 5-iodo-2,4-dimethylselenophen were obtained from 6.7 g (0.042 mole) 2,4-dimethylselenophen* (b.p. 154.5–155.5 at 726 mm, n_D^{20} 1.5498, d_4^{20} 1.3672), 10.7 g (0.042 mole) iodine and 7.5 g (0.033 mole) of yellow mercuric oxide in 25 ml anhydrous benzene:

B. p. 115–116° (14 mm), n_D^{20} 1.6455, d_4^{20} 2.0402, MR_D 50.44; calc. 50.18.
Found %: C 25.63, 25.54; H 2.60, 2.62. C_6H_7ISe. Calculated %: C 25.28; H 2.48.

* The 2,4-dimethylselenophen prepared by us is not described in the literature.

2-Iodo-3,4-dimethylselenophen. 3.6 g unchanged 3,4-dimethylselenophen and 7.5 g (52%, calculated from the 3,4-dimethylselenophen which had reacted) 2-iodo-3,4-dimethylselenophen were obtained from 11 g (0.07 mole) 3,4-dimethylselenophen, 17.5 g (0.07 mole) iodine and 12 g (0.05 mole) yellow mercuric oxide in 30 ml anhydrous benzene:

B. p. 122–123° (12 mm), n_D^{20} 1.6478, d_4^{20} 2.0662, MR_D 50.17; calc. 50.18.

Found %: C 25.78, 25.56; H 2.60, 2.62. C_6H_7ISe. Calculated %: C 25.58; H 2.48

II. Metallation of the Selenophen Nucleus and Preparation of Selenophen Carboxylic Acids

An ether solution of the iodoselenophen was added dropwise in an atmosphere of nitrogen (with mechanical stirring) to a solution of phenyllithium prepared by the reaction of bromobenzene with lithium in absolute ether. The reaction mixture was then heated on the water bath for 15 minutes, cooled well and pieces of solid carbon dioxide were added until the ether had stopped boiling. The reaction mixture was decomposed with water with a few drops of concentrated hydrochloric acid added and the ether solution separated from the aqueous solution. The aqueous solution of the lithium salt of the selenophen carboxylic acid was evaporated to small volume (15-20 ml), acidified with 20% hydrochloric acid and the white flaky precipitate of the acid which formed was separated. The acid was recrystallized from water or dilute alcohol.

Selenophen-2-carboxylic acid. 5 g (0.02 mole) 2-iodoselenophen, 7.5 g (0.05 mole) bromobenzene and 0.7 g (0.1 mole) lithium gave 2 g (57%) selenophen-2-carboxylic acid: m.p. 119-120° (from water).

Found %: C 34.65, 34.70; H 2.61, 2.52. $C_5H_4O_2Se$. Calculated %: C 34.32; H 2.30.

Literature data: m.p. 122-124° [3], m.p. 120° [9].

3-Methylselenophen-2-carboxylic acid. 3.8 g (0.014 mole) 2-iodo-3-methylselenophen, 5.7 g (0.036 mole) bromobenzene and 0.49 g (0.07 mole) lithium gave 1.3 g (50%) 3-methylselenophen-2-carboxylic acid: m.p. 133-134° (from water).

Found %: C 38.12, 37.98; H 3.38, 3.32. $C_6H_6O_2Se$. Calculated %: C 38.11; H 3.20.

2,4-Dimethylselenophen-5-carboxylic acid. 3 g (0.01 mole) 5-iodo-2,4-dimethylselenophen, 4 g (0.025 mole) bromobenzene, 0.35 g (0.05 mole) lithium gave 1.1 g (52%) 2,4-dimethylselenophen-5-carboxylic acid: m.p. 177-177.5° (decomp.) (from dilute alcohol).

Found %: C 41.69, 41.70; H 4.11, 4.19. $C_7H_8O_2Se$. Calculated %: C 41.40; H 3.97.

3,4-Dimethylselenophen-2-carboxylic acid. 6.5 g (0.023 mole) 2-iodo-3,4-dimethylselenophen, 9.4 g (0.06 mole) bromobenzene and 0.77 g (0.11 mole) lithium gave 2.8 g (61%) 3,4-dimethylselenophen-2-carboxylic acid: m.p. 183.5-184° (decomp.) (from dilute alcohol).

Found %: C 41.71, 41.58; H 3.75, 3.74. $C_7H_8O_2Se$. Calculated %: C 41.40; H 3.97.

SUMMARY

1. The selenophen nucleus is easily iodinated by the action of iodine in the presence of yellow mercuric oxide. The following compounds, which are not described in the literature, have been prepared in this way: 2-iodo-3-methylselenophen, 5-iodo-2,4-dimethylselenophen and 2-iodo-3,4-dimethylselenophen; and also 2-iodoselenophen.

2. The selenophen nucleus is easily metallated by the reaction of phenyllithium on th iodides of the selenophen series. On subsequent carbonation of the lithiumselenophens the carboxylic acids of the selenophen series are obtained. The following compounds, which have not been described in the literature, have been prepared in this way: 3-methylselenophen-2-carboxylic acid, 2,4-dimethylselenophen-5-carboxylic acid and 3,4-dimethylselenophen-2-carboxylic acid; and also selenophen-2-carboxylic acid.

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43. SYNTHETIC PAIN-RELIEVING SUBSTANCES. VII. 1-ALKYL-2,5-DIMETHYL-4-PHENYL-4-PIPERIDINOLS

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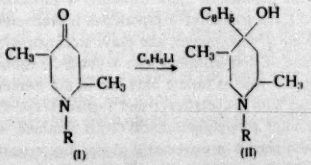
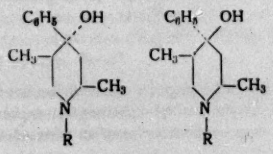
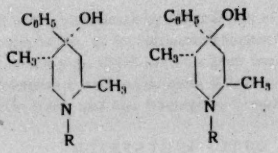
The synthesis of 4-phenyl-4-piperidinols is of considerable interest in connection with the fact that several of their esters exhibit a powerful pain-relieving action. Promedol and isopromedol, which have been synthesized in our laboratory, are the propionic esters of the stereoisomeric 1,2,5-trimethyl-4-phenyl-4 piperidinols (II, R = CH_3) and are among the most powerful and interesting present-day analgesics. As we had at our disposal a series of 1-alkyl-2,5-dimethyl-4-piperidones (I), which have been described in previous communications [1], we decided to synthesize from them the corresponding 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II), whose propionic esters are the homologs of promedol and isopromedol and which differ from the latter only in the substituents on the nitrogen. The crystalline 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) are formed in good yield (70-80%) by the action of phenyllithium on 1-alkyl-2-5-dimethyl-4-piperidones (I). The molecule of the former contains three asymmetric carbon atoms and they may exist in four geometric isomeric forms.



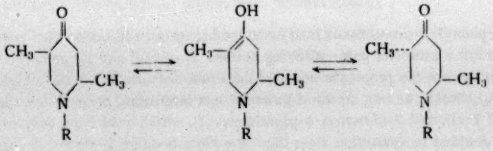
R=CH_3, C_2H_5, C_3H_7, iso-C_3H_7, C_4H_9, C_5H_{11}, iso C_5H_{11}, iso-C_5H_{11}, cyclo-C_6H_{11}.

It turned out, however, that the spatial directivity of the reaction of phenyllithium with 2,5-dimethyl-4-piperidones depends to a great extent on the nature of the substituent on the nitrogen of the piperidine nucleus. In the reaction of phenyllithium with 1-alkyl-2,5-dimethyl-4-piperidones (I), where the alkyl substituents are small aliphatic radicals (methyl, ethyl, propyl, isopropyl, allyl), it is possible in every case to isolate three of the stereoisomeric 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II), from the four theoretically possible.



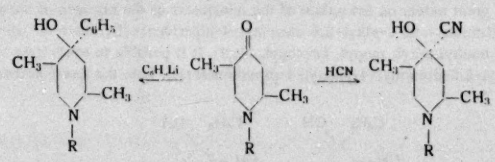


At the same time, in all cases the high-melting γ-isomers predominate in the mixture, while the α- and β-isomers are usually obtained in small amount and the fourth isomer is evidently not formed at all. The fact that three stereoisomers out of the four theoretically possible are isolated provides evidence that in this case the piperidones (I) react with phenyllithium in both their stereoisomeric forms (cis-and trans-), which exist in a state of tautomeric equilibrium with the enolic form.



In this connection it is interesting to note that γ-piperidones react with Grignard reagents predominantly as the enolic form, which explains the low yield of tertiary γ-piperidinols obtained in this way.

Thus, for example, ethane is liberated violently in almost quantitative yield from the reaction of 1,2,5-trimethyl-4-piperidone with ethyl magnesium bromide, and after the usual treatment approximately 60% of the original piperidone is recovered. In the reaction of 1,2,5-trimethyl-4-piperidone with phenyl magnesium bromide approximately 80% of unreacted 1,2,5-trimethyl-4-piperidone is recovered [2]. Thus, a high tendency to enolize is a characteristic property of the γ-piperidones, and plays an important part in their reversible cis-trans isomeric changes. In the reaction of phenyllithium with 1-butyl-, 1-isobutyl-and 1-isoamyl-2,5-dimethyl-4-piperidones we were able in each case to isolate only two of the stereoisomeric phenylpiperidinols (II), while in the reaction of phenyllithium with 1-cyclohexyl-and 1-phenyl-2,5-dimethyl-4-piperidones only one of the spatial isomers of the corresponding phenylpiperidinols (II) is obtained in good yield (60-80%). Consequently, when such substituents as the phenyl or cyclohexyl groups are present on the nitrogen of the piperidine nucleus, the reaction of phenyllithium and 2,5-dimethyl-4-piperidones becomes spatially selective, as in the case of the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones. In contrast to phenyllithium, the addition of hydrogen cyanide is spatially selective with all 1-alkyl-2,5-dimethyl-4-piperidones (irrespective of the substituent on the nitrogen), where the screening effect is shown, in all probability, by the methyl group next to the carbonyl group. An important conclusion from the observations



described is that a screening effect on the carbonyl group can be shown not only by neighboring substituents but also by radicals bound to the nitrogen. All the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols described in the present communication were prepared by us by the addition of an ether solution of the 1-alkyl-2,5-dimethyl-

4-piperidones to a cooled solution of phenyllithium taken in 20-50% excess. After being heated for three hours, the reaction mass was decomposed with water and the ether layer separated and dried with sodium sulfate. After the ether had been distilled off, the high-melting γ-isomer of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinol which predominates in the mixture was precipitated and purified by recrystallization from benzene boiling at 80-120°. The mixture of isomers which did not crystallize was vacuum distilled and separated, usually as the hydrochlorides, by fractional crystallization from alcohol or from a mixture of alcohol and ether. The hydrochlorides of the high-melting γ-isomers of all the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols had lower melting points and were more difficult to crystallize than the hydrochlorides of the α- and β-isomers. The identity of spatial structure of the homologs of each series was confirmed by a comparison of the physiological properties of their propionates. The hydrochlorides of the propionates of the β-isomers of all the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols are much more active analgesics than the derivatives of the γ-isomers. The identity of spatial structure of the α-, β- and γ-isomers of 1-allyl- and 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinols was established by hydrogenation of the allyl derivatives to the corresponding propyl derivatives in the presence of Raney nickel catalyst. On hydrogenation of the high-melting γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol, the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol is formed, while hydrogenation of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol leads to the formation of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. On hydrogenation of the oily mixture of isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol a mixture of products was obtained, from which it was possible to isolate the α-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol.

EXPERIMENTAL

The original 1-alkyl-2,5-dimethyl-4-piperidones (I) were obtained by the action of primary amines on propenyl isopropenyl ketone and the corresponding methoxy ketones, as described earlier [1].

1,2,5-Trimethyl-4-phenyl-4-piperidinol (II, R = CH_3). 500 ml absolute ether was placed in a three-necked flask fitted with a stirrer, reflux condenser, thermometer, dropping funnel and tube for the admission of gas, and 45.8 g of finely divided lithium, purified from oxide layer, was added in a current of dry nitrogen. 20 g bromobenzene was then poured in an atmosphere of dry nitrogen into the mixture and when violent reaction had begun 498 g bromobenzene in 550 ml absolute ether solution was added dropwise at such a rate that the ether was kept constantly boiling. When all the bromobenzene had been added the reaction mass was stirred, with the ether boiling, for one and a half hours until the lithium had dissolved completely. 352 g 1,2,5-trimethyl-4-piperidone (I, R = CH_3), (b.p. 73-75° at 7 mm) [3] in 550 ml absolute ether was added dropwise to the solution of phenyllithium obtained over a period of two hours with cooling in a mixture of ice and salt (-6°). The reaction mass was left overnight and stirred on the following day for two hours with the ether boiling, then cooled to room temperature and hydrolyzed with water (400 ml).

The ether layer was removed, the aqueous layer extracted with ether, the ether extracts dried with magnesium sulfate and after distillation of the ether the volatile products were removed at 10 mm pressure on a boiling water bath. The residue (500 g) was dissolved by heating in 150 ml benzine (b.p. 80-120°), the solution was cooled and left overnight. The next day 127.4 g of crystals of the high-melting γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol (II, R = CH_3) had separated, with m.p. 107.5-108° (from benzine), giving no depression on taking mixed melting points with the specimen described earlier [4]. The hydrochloride of this isomer melted at 158-160° (from alcohol and ether). On evaporation of the mother liquors a further 24.3 g of the γ-isomer with m.p. 108-109° was isolated. The uncrystallized oil which remained after the separation of the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol was dissolved in concentrated hydrochloric acid (220 ml), extracted with ether, saturated with solid caustic potash, extracted with ether, dried with ignited sodium sulfate and vacuum distilled. 52.3 g of the original 1,2,5-trimethyl-4-piperidone, b. p. 80-85° at 15 mm, and 218 g of II, b. p. 122-152° at 0.7 mm were obtained, and from the latter 13.3 g of the γ-isomer, m. p. 108-109°, was separated by addition of benzine (250 ml). Evaporation of the mother liquors gave 94.5 g of a crystalline mixture of isomers of II, m. p. 79-90°.

The uncrystallized part of the mixture was vacuum distilled and 40 g of a crystalline mixture (m.p. 73-81°) of isomers was obtained from the fraction distilling at 102-134° and 1 mm (96 g), by the addition of benzine. The oily residue (53g) obtained on evaporating the benzine mother liquor was dissolved in 200 ml of absolute ether and saturated with dry hydrogen chloride. On recrystallization of the precipitate of isomeric 1,2,5-trimethyl-

4-phenyl-4-piperidinol hydrochlorides (60 g) obtained, from alcohol and acetone, 16.5 g of the hydrochloride of the α-isomer with m.p. 229-230° was obtained, and from this 14.5 g of the free base with m.p. 106-107° was obtained by the action of ammonia [2]. The residue after the separation of the α-isomer hydrochloride was converted into a mixture of the bases, from which 7.4 g of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 102-103° was obtained by recrystallization from benzine [2]. A further 1.8 g of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol, m.p. 102-103°, was obtained from the crystalline mixture of isomeric 1,2,5-trimethyl-4-phenyl-4-piperidinol bases with m.p. 73-90° (135 g), by repeated fractional crystallization from benzine; the part of the mixture remaining could not be separated.

This experiment yielded in all: 165 g γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 108-109°, 9.2 g β-isomer 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 102-103° and 14.5 g α-isomer 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 106-107°. In addition, 133 g of a crystalline mixture of isomeric 1,2,5-trimethyl-4-phenyl-4-piperidinols was not separated.

The action of ethyl magnesium bromide on 1,2,5-trimethyl-4-piperidone. A solution of 21.3 g 1,2,5-trimethyl-4-piperidone (b.p. 75-76° at 9 mm) in 25 ml absolute ether was added dropwise with vigorous shaking over a period of 1 hour to a solution of ethyl magnesium bromide prepared from 7.2 g magnesium and 33 g ethyl bromide in 90 ml absolute ether. During the addition of the piperidone 3 liters of ethane was evolved; when the reaction mass was subsequently heated for 15 minutes until the ether boiled, no further evolution of ethane took place and a thick white precipitate of the magnesium bromoenolate of 1,2,5-trimethyl-4-piperidone was formed. The reaction mass was then decomposed with caustic potash solution (100 ml 30% solution), saturated with caustic potash, extracted with ether, dried with caustic potash and vacuum distilled. 14 g of the original 1,2,5-trimethyl-4-piperidone with b.p. 75-80° at 9 mm and 2.5 g 1,2,5-trimethyl-4-ethyl-4-piperidinol with b.p. 105-110° at 9 mm [4] were obtained. The residue in the distillation flask amounted to 2 g.

1-Ethyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = C_2H_5). A solution of 140 g 1-ethyl-2,5-dimethyl-4-piperidone (b.p. 76-78° at 6 mm) [1] in 280 ml absolute ether was added with cooling by a mixture of ice and salt (-10°) over a period of 5.5 hours to a solution of phenyllithium prepared from 15 g metallic lithium and 170 g bromobenzene in 1000 ml absolute ether. The reaction mass was left overnight, then heated for 3 hours with the ether boiling and treated with water (400 ml). The ether layer was separated, the aqueous layer extracted with ether, the ether extracts combined and dried with sodium sulfate. After distillation of the ether and addition of benzine (b.p. 80-100°) to the residue, 114.8 g of a crystalline mixture of the isomers of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 76.5-92° was isolated. 44.5 g of the high-melting γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 101-101.5° was obtained from this mixture after five recrystallizations from benzine.

Found %: N 6.34, 6.15. $C_{15}H_{23}ON$. Calculated %: N 6.01.

The hydrochloride of this piperidinol, obtained in the usual way, melted at 190°.

Found %: Cl 13.28, 13.40. $C_{15}H_{24}ONCl$. Calculated %: Cl 13.16.

On evaporation of the mother liquors left after the separation of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol, 53 g of the mixed isomers of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol was isolated as colorless crystals with m.p. 77-83°. This mixture was converted to the hydrochloride by passing dry hydrogen chloride into a solution of the bases in ether. After two recrystallizations from a mixture of alcohol and ether, 25 g of the hydrochloride of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 212° was obtained.

Found %: Cl 13.26, 13.38. $C_{15}H_{24}ONCl$. Calculated %: Cl 13.16.

21.4 g of this hydrochloride was dissolved in water, saturated with sodium carbonate, the bases extracted with ether and dried with sodium sulfate and, after distillation of the ether, recrystallized from benzine. 17 g of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 97° was obtained.

Found %: N 5.89, 5.83. $C_{16}H_{23}ON$. Calculated %: N 6.01.

A mixture of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 97°) with the γ-isomer of this compound (m.p. 101-101.5°) melted at 77.5-81°.

The mother liquors left after the separation of the β-and γ-isomers of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol were extracted with 10% hydrochloric acid solution (120 ml), saturated with alkali, extracted with ether, dried with sodium sulfate and vacuum distilled: the 1st fraction, b.p. 59-117° at 1 mm, amounted to 14.6 g; the 2nd fraction, b.p. 117-137° at 1 mm, amounted to 44.8 g; 5 g of residue remained in the distillation flask.

After the addition of benzine (b.p. 80-100°) and freezing, the 2nd fraction yielded 24.8 g of a mixture of isomeric 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinols in the form of colorless crystals with m.p. 77-79°. The uncrystallized part was again vacuum distilled. 6.3 g of an oily mixture of isomeric 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinols was obtained and converted to the hydrochloride by the passage of dry hydrogen chloride into a solution of the bases in benzine. 1 g of the hydrochloride of the low-melting α-form of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 211-212° was obtained by repeated recrystallization from alcohol.

Found %: N 5.57, 5.51; Cl 13.38, 13.29. $C_{16}H_{24}ONCl$. Calculated %: N 5.19; Cl 13.36.

A mixture with the hydrochloride of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol described above (m.p. 212°) melted at 188-194°. 0.8 g of the hydrochloride of the α-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-piperidinol (melting point 211-212°) was dissolved in water, the solution saturated with sodium carbonate, the product extracted with ether, dried with sodium sulfate and, after distillation of the ether, recrystallized from benzine. 0.5 g of the low-melting α-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol was obtained with m.p. 91°.

Found %: N 6.26, 6.16. $C_{16}H_{23}ON$. Calculated %: N 6.01.

Mixtures of the α-form of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with the β-and γ-forms melted at 73-77°and 72-79° respectively.

The experiment yielded in all: 44.5 g of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 101-101.5°, 21.6 g of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 97°, 0.8 g of the α-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 91°. Approximately 80 g of residual material remained as an unseparated mixture of stereoisomers.

1-Propyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = C_3H_7). 150 g 1-propyl-2,5-dimethyl-4-piperidone (b.p. 80-82° at 5 mm) [1] in 200 ml absolute ether was added with cooling by a mixture of ice and salt (-10°) and uninterrupted stirring over a period of 4 hours to a solution of phenyllithium prepared from 18 g of metallic lithium and 204 g bromobenzene in 850 ml absolute ether. The reaction mass was left overnight and then stirred for 3 hours with the ether boiling and treated with water (200 ml). The ether layer was separated, a further 200 ml of water added to the residue to break up the emulsion and the aqueous layer extracted with ether (200 ml). The ether extracts were combined and extracted with 10% hydrochloric acid (300 ml). After distillation of the ether from the ether layer, 16 g of neutral products was obtained in the form of a dark oil. The hydrochloric acid extract of the bases was saturated with potassium carbonate, extracted with ether and dried with sodium sulfate. After distillation of the ether the residue crystallized. 54 g of the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 93-94° was obtained after five recrystallizations from benzine (b.p. 80-100°).

Found %: N 5.58, 5.37. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The hydrochloride of this piperidinol, prepared in the usual way, melted at 174-175° (from a mixture of alcohol and ether).

Found %: Cl 12.25, 12.41. $C_{16}H_{26}ONCl$. Calculated %: Cl 12.55.

The picrate melted at 173-174° after two recrystallizations from alcohol.

The methiodide formed colorless crystals with m.p. 281-282° (from alcohol).

Found %: N 3.82, 3.91. $C_{17}H_{28}ONI$. Calculated %: N 3.58.

The mother liquors from the separation of the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°) were vacuum distilled: 1st fraction, b.p. 70-125° at 2.5 mm, 5 g; 2nd fraction, b.p. 126-146° at 2.5 mm, 91 g; 3rd fraction, b.p. 175-185° at 2.5 mm, 2 g. Residue in distillation flask 15 g.

After standing for a number of days the second fraction on freezing yielded 55 g of a mixture of the isomeric 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinols in the form of colorless crystals with m.p. 45-90°. This mixture was converted to the hydrochlorides by passing dry hydrogen chloride into an ether solution of the bases. After repeated recrystallization from alcohol 50 g of coarse colorless prismatic hydrochloride crystals with m.p. 201.5-202° was separated, corresponding to the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol.

Found %: N 4.87, 5.16; Cl 12.20, 11.90. $C_{16}H_{26}ONCl$. Calculated %: N 4.95; Cl 12.55.

2 g of the hydrochloride described above (m.p. 201.5-202°) was dissolved in 20 ml water and treated with 5 ml concentrated aqueous ammonia solution. The oil which separated was crystallized. The β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol thus obtained melted at 53.5-55° (from benzine).

Found %: N 5.76, 5.68. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The picrate melted at 119-120° (from alcohol).

Found %: N 11.80, 12.00. $C_{22}H_{28}O_8N_4$. Calculated %: N 11.80

Evaporation of the mother liquors from the separation of the hydrochloride of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 201.5-202°) and precipitation with ether yielded 8 g of the hydrochloride of the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 174-175°, which gave no depression on taking mixed melting points with the specimen described above. 35 g of the liquid mixture of isomers of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol remaining from the 2nd fraction was converted to the hydrochlorides, which yielded 14 g of the hydrochloride of the β-isomer with m.p. 201.5-202°, giving no depression on taking mixed melting points with the specimen described above. Evaporation of the mother liquors and precipitation with ether yielded 10 g of a crystalline mixture of hydrochlorides with m.p. 121-160°. Five recrystallizations of this mixture from a mixture of alcohol and ether yielded 2 g of an individual hydrochloride, m.p. 193-195°, which corresponds to the liquid α-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol.

Found %: Cl 12.05, 12.45; N 4.94, 5.23. $C_{16}H_{26}ONCl$. Calculated %: Cl 12.55; N 4.95.

1.5 g of this hydrochloride (m.p. 193-195°) was dissolved in 20 ml of water and treated with 10 ml of concentrated aqueous ammonia solution. The oil which separated was extracted with ether, dried with sodium sulfate and distilled in vacuo. 1 g of the liquid α-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 124-125° at 2.5 mm was obtained in the form of a viscous oil which could not be crystallized.

Found %: N 5.81, 5.25. $C_{16}H_{25}ON$. Calculated %: N 5.65.

The experiment yielded in all: 61 g of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 93-94°, 43.5 g of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 53.5-55°, 1.8 g of the α-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (as an oil).

1-Allyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = C_3H_5). 139 g of 1-allyl-2,5-dimethyl-4-piperidone (b.p. 85-87° at 7 mm) [1], in 250 ml absolute ether was added with cooling by a mixture of ice and salt (-10°) and uninterrupted stirring over a period of 4 hours to a solution of phenyllithium prepared from 12.5 g of metallic lithium and 132 g bromobenzene in 700 ml absolute ether. The reaction mass was left overnight and then stirred for 3 hours with the ether boiling and treated with 10% hydrochloric acid (200 ml). The ether layer was separated and extracted thrice with 10% hydrochloric acid (200 ml in all). The hydrochloric acid extracts were combined, saturated with solid caustic potash, the oil which separated extracted with ether, dried with sodium sulfate and vacuum distilled: 1st fraction, b.p. 90-133° at 4 mm, 20 g; 2nd fraction, b.p. 133-150° at 4 mm, 130 g. Residue in the distillation flask 30 g.

The second fraction, a mixture of the isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol, was crystallized by the addition of benzine (b.p. 80-100°). After seven recrystallizations from benzine 18 g of the high-melting γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol was obtained, with m.p. 93-94°.

Found %: N 5.77, 5.44. $C_{16}H_{23}ON$. Calculated %: N 5.71.

No crystalline hydrochloride of the γ-isomer could be obtained. The allylbromide melted at 210-211° (from alcohol).

Found %: N 4.02, 3.93. $C_{19}H_{28}ONBr$. Calculated %: N 3.82.

Evaporation and freezing of the mother liquors from the separation of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol yielded 22 g of a crystalline mixture of isomers with m.p. 67-74°. On distilling the oily residue in vacuo, 85 g of a fraction with b.p. 133-144° at 4 mm was collected, and from this fraction 10 g of a crystalline mixture of the isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 68-74° was obtained by addition of benzine and freezing. All the crystalline fractions with m.p. 67-74° were combined (32 g) and recrystallized from benzine. 23 g of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 71-72° was obtained.

Found %: N 5.94, 6.02. $C_{16}H_{23}ON$. Calculated %: N 5.71.

The hydrochloride of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 186-187° (from alcohol).

The mother liquors from the separation of the β- and γ-isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol were combined, evaporated and vacuum distilled. 80 g of a mixture of isomers was obtained, which on prolonged standing yielded 20 g of the β-isomer with m.p. 71-75° (from benzine). The residual part of the material (about 60 g) remained as a mixture of the isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol which did not crystallize. As can be seen from the hydrogenation results (see below) this mixture contained, in addition to the crystalline β- and γ-isomers with m.p. 71-72° and 93-94° described above, the α-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol.

This experiment yielded in all: 18 g of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 93-94°, 43 g of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 71-72°, 60 g of an unseparated mixture of the isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol.

The hydrogenation of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol. a) 2 g of the high-melting γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°) was hydrogenated in solution in 30 g methanol over Raney nickel. In 40 minutes 200 ml hydrogen (21°, 750 mm) was absorbed, as against 201 ml required theoretically. The catalyst was filtered off, the methanol distilled and the residue recrystallized from benzine (b.p. 80-100°), 1.6 g of the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-piperidinol with m.p. 93-94° was obtained and gave no depression of the melting point with the specimen described above. A mixed melting

point with the original 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°) melted at 83-87°, i.e., gave a pronounced depression.

b) 6 g of the unpurified β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m. p. 71-73°) was hydrogenated in solution in 100 ml methanol over Raney nickel. In 40 minutes 620 ml hydrogen (24°, 758 mm) was absorbed, as against 614 ml required theoretically. The catalyst was filtered off, the methanol distilled and the residue dissolved in hot benzine (b.p. 80-100°). When the solution was cooled, 0.6 g of the high-melting γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol, m.p. 93-94°, was obtained and this gave no melting point depression with the specimen described above. The mother liquor from the separation of the high-boiling γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol was vacuum distilled. 4.5 g of oil with b.p. 123-126° at 2.5 mm was obtained and converted to the hydrochloride in the usual way. On recrystallization from a mixture of alcohol and ether 3 g of the hydrochloride of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 201-202° was obtained, giving no melting point depression with the specimen described above.

c) 16 g of the uncrystallized mixture of the isomers of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol remaining after the separation of the crystalline β- and γ-isomers was hydrogenated in solution in 160 ml methanol over Raney nickel. In 5 hours 1700 ml of hydrogen (21°, 750 mm) was absorbed as against 1630 ml required theoretically. The catalyst was filtered off, the methanol distilled and the residue dissolved in benzine (3 g of dark tarry material did not dissolve in the benzine). After the benzine had been distilled off the residue was vacuum distilled. 12 g of a mixture of the isomers of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol was obtained as a viscous oil with b.p. 123-126° at 2.5 mm, and converted into the hydrochloride in the usual way. Repeated recrystallization from a mixture of alcohol and ether yielded 4 g of the hydrochloride of the liquid α-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 193-195°, giving no depression with the specimen described above.

1-Isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = iso-C_3H_7). A solution of 177 g 1-isopropyl-2,5-dimethyl-4-piperidone (b.p. 75-80° at 3.5 mm) [1] in 300 ml ether was added with cooling by a mixture of ice and salt (-10°) over a period of 6 hours with uninterrupted stirring to a solution of phenyllithium prepared from 16 g lithium and 180 g bromobenzene in 700 ml absolute ether. On the next day the mixture was stirred for three hours with the ether boiling and then hydrolyzed with 500 ml of cold water. The ether layer was separated, dried with sodium sulfate, the ether distilled off and the residue vacuum distilled. This produced 170 g of a mixture of the isomers of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 137-150° at 6 mm, from which 80 g of crystals with m.p. 87-95° was separated by the addition of an equal volume of benzine. Two recrystallizations from benzine yielded 55 g of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 106-107°.

Found %: N 5.74, 5.69. $C_{16}H_{25}ON$. Calculated %: N 5.65.

On evaporation of the mother liquors and seeding, a further 25 g of the γ-isomer with m.p. 106-107° was obtained. The hydrochloride of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 216-218°. The uncrystallized oil remaining after the separation of the γ-isomer was dissolved in double its volume of benzine and saturated with dry hydrogen chloride. Recrystallization of the precipitated hydrochlorides from alcohol yielded 34 g of the hydrochloride of the β-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 268-270°. The free base of the β-isomer, separated in the usual way, melted at 67-69°.

Found %: N 5.25, 5.54. $C_{16}H_{25}ON$. Calculated %: N 5.65.

10 times the volume of dry ether was added to the alcoholic mother liquors remaining after the separation of the hydrochloride of the β-isomer. The precipitate obtained was converted to the base and recrystallized from benzine. 6 g of the α-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 63-65° was obtained.

Found %: N 5.50, 5.66. $C_{16}H_{25}ON$. Calculated %: N 5.65.

The hydrochloride of the α-isomer melted at 236-238°. A mixture of the α- and β-isomers melted at 20-40°. This experiment yielded in all: 80 g of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 106-107°, 30 g of the β-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 67-69°, 6 g of the α-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 63-65°. 20 g of an unseparated mixture of isomers was left in the form of a viscous oil.

1-Butyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = N-C_4H_9). 101 g 1-butyl-2,5-dimethyl-4-piperidone (b.p. 80-85° at 4 mm) [4] in 100 ml ether was added with cooling by a mixture of ice and salt (-10°) and un-interrupted stirring over a period of 4 hours to a solution of phenyllithium prepared from 9 g of lithium and 94 g of bromobenzene in 600 ml of ether. The reaction mass was left overnight and warmed on the next day for 3 hours until the ether boiled, cooled and decomposed with 200 ml of water. The ether layer was separated, the ether distilled off, the residue treated with 10% hydrochloric acid (200 ml) and left overnight. 100 g of a crystalline mixture of the isomeric hydrochlorides of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 90-150° was obtained. The hydrochloric acid filtrate was treated with ammonia, extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 15 g of an oily mixture of the isomers of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 135-145° at 3.5 mm, from which 10 g of a crystalline mixture of the hydrochlorides with m.p. 100-160° was obtained in the usual way. The hydrochlorides isolated in this way were combined and subjected to repeated fractional crystallization from alcohol. 18 g of the hydrochloride of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol was obtained, with m.p. 193-194.5°.

Found %: N 4.82, 4.80. $C_{17}H_{28}ONCl$. Calculated %: N 4.70.

The β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 71-72°.

Found %: C 77.93; H 10.32. $C_{17}H_{27}ON$. Calculated %: C 78.16; H 10.34.

Evaporation of the alcoholic mother liquors from the separation of the hydrochloride of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol and addition of ether yielded 60 g of a mixture of the hydrochlorides of the isomeric 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinols with m.p. 145-180°. Recrystallization of this mixture from a mixture of alcohol and acetone yielded 39 g of the hydrochloride of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with m. p. 161-162°.

Found %: Cl 11.72. $C_{17}H_{28}ONCl$. Calculated %: Cl 11.90.

The γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 96-96.5°.

Found %: C 77.96 H 10.20. $C_{17}H_{27}ON$. Calculated %: C 78.16; H 10.34.

This experiment yielded in all: 34.5 g of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 96-96.5°, 16 g of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 71-72°, 50 g of an unseparated mixture of isomers with m.p. 50-60° (the hydrochlorides melted at 145-185°).

1-Isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = iso-C_4H_9). 129 g 1-isobutyl-2,5-dimethyl-4-piperidone (b.p. 85-90° at 5 mm) [1] in 250 ml absolute ether was added with cooling by a mixture of ice and salt (-10°) over a period of 5 hours to a solution of phenyllithium prepared from 12 g of metallic lithium and 140 g bromobenzene in 400 ml absolute ether. When all the piperidone had been added, the reaction mass was left overnight and stirred on the next day for 3 hours with the ether boiling, then cooled to 0° and treated with water (400 ml). The ether layer was separated, washed twice with water, dried with sodium sulfate and saturated with dry hydrogen chloride. When the mixture of hydrochlorides of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol which precipitated was recrystallized from a mixture of alcohol and ether 65 g of the hydrochloride of the β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 219-220° was

obtained. The β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol, separated from the hydrochloride by the action of concentrated aqueous ammonia, had b.p. 149-150° at 3 mm, m.p. 27-29°.

Found %: N 5.46, 5.63. $C_{17}H_{27}ON$. Calculated %: N 5.36.

The alcohol-ether mother liquors from the recrystallization of the hydrochloride of the β-isomer were evaporated in vacuo, the residue dissolved in water and treated with concentrated aqueous ammonia. Recrystallization of the bases obtained from benzine (b.p. 80-100°), yielded 40 g of the γ-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 72-73°.

Found %: N 5.23, 5.27. $C_{17}H_{27}ON$. Calculated %: N 5.36.

The hydrochloride of the γ-isomer of 1- isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 180-181°.

Evaporation of the mother liquors from the recrystallization of the γ-isomer yielded 11 g of an oily mixture of the isomers of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 135-137° at 3.5 mm.

This experiment yielded in all: 40 g of the γ-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 72-73°, 57 g of the β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 27-29°, 11 g of an oily mixture of the isomers of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 135-137° at 3.5 mm.

1-Isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = iso-C_5H_{11}). A solution of 240 g 1-isoamyl-2,5-dimethyl-4-piperidone (b.p. 95-100° at 5 mm) [1] in 250 ml absolute ether was added with uninterrupted stirring over a period of 6 hours with cooling by a mixture of ice and salt (-10°) to a solution of phenyllithium prepared from 24 g of metallic lithium and 280 g bromobenzene in 800 ml ether. The reaction mass was left overnight and stirred on the next day for 3 hours with the ether boiling, cooled to 0° and decomposed with water (500 ml). The ether layer was separated and treated with 10% hydrochloric acid (500 ml). The hydrochloric acid solution and the oily mixture of the isomeric hydrochlorides of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol which had separated were treated with concentrated aqueous ammonia, extracted with ether and dried with sodium sulfate. The ether was distilled off and 50 ml benzine (b.p. 80-100°) added to the residue to precipitate 30 g of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 109-110° (from benzine).

Found %: N 5.01, 4.99. $C_{18}H_{29}ON$. Calculated %: N 5.10.

The hydrochloride of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 112-118° (from a mixture of alcohol and ether).

The oily residue from the separation of the γ-isomer was vacuum distilled. This yielded 200 g of a mixture of the isomers of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 145-170° at 3 mm, from which a further 53 g of the γ-isomer with m.p. 109-110° was separated by repeated recrystallization from benzine.

Evaporation of the mother liquors from the separation of the γ-isomer yielded 85 g of a crystalline mixture of the isomers of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 65-75°, which was converted to the hydrochloride in the usual way. Repeated recrystallization of the resultant mixture of hydrochlorides from a mixture of alcohol and ether yielded 70 g of the hydrochloride of the β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 182-183.5°. The β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol melted at 83-84°.

Found %: N 5.44, 5.40. $C_{18}H_{29}ON$. Calculated %: N 5.10.

This experiment yielded in all: 83 g of the γ-isomer of 1-isoamyl-2,5- dimethyl-4-phenyl-4-piperidinol with m.p. 109-110°, 62 g of the β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 83-84°, 65 g of an oily mixture of the isomers of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 145-150° at 3.5 mm.

1-Cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol (R = cyclo-C_6H_{11}). 60 g of 1-cyclohexyl-2,5-dimethyl-4-piperidone in 200 ml absolute ether was added dropwise with cooling by a mixture of ice and salt (-10°) over a period of 4 hours to a solution of phenyllithium prepared from 6 g of lithium and 68 g bromobenzene in 300 ml absolute ether. The reaction mass was left overnight, then heated for 3 hours with the ether boiling and treated with water (100 ml). The ether layer was separated and dried with sodium sulfate. After distillation of the ether the residue was recrystallized twice from benzine (b.p. 80-100°). 40 g of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 114.5-115° was obtained.

Found %: N 5.10, 4.71. $C_{19}H_{29}ON$. Calculated %: N 4.88.

The mother liquors from the separation of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol were vacuum distilled: 1st fraction, b.p. 70-170° at 3 mm, 4.5 g; 2nd fraction, b.p. 170-190° at 3 mm, 33 g. Residue in distillation flask 5 g.

Thus, in this reaction it was possible to isolate only one isomer of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol in contrast to the reactions described above with 1-methyl-, 1-ethyl-, 1-propyl-, 1-isopropyl- and 1-allyl-2,5-dimethyl-4-piperidones, in which, in each case, three spatial isomers of the corresponding 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols were formed. As has been shown earlier [5], the reaction of phenyllithium with 1-phenyl-2,5-dimethyl-4-piperidone also leads to an 80% yield of only one spatial isomer of 1,4-diphenyl-2,5-dimethyl-4-piperidinol.

1-Benzyl-2,5-dimethyl-4-phenyl-4-piperidinol (II, R = $CH_2C_6H_5$). 13 g 1-benzyl-2,5-dimethyl-4-piperidone (b.p. 129-130° at 3.5 mm) [1] in 20 ml absolute ether was added with cooling by a mixture of ice and salt over a period of 4 hours to a solution of phenyllithium prepared from 0.9 g metallic lithium and 9.4 g bromobenzene in 100 ml absolute ether. The reaction mass was stirred for one and a half hours at room temperature, then treated with water (30 ml) and concentrated hydrochloric acid (100 ml). The hydrochloric acid solution was saturated with sodium carbonate, extracted with ether, dried with sodium sulfate and vacuum distilled: 1st fraction, b.p. 115-134° at 2.5 mm, 22 g; 2nd fraction, b.p. 130-173° at 2.5 mm, 6 g. Residue in flask 1 g. Distillation of the 2nd fraction yielded 3.5 g of a mixture of isomers of 1-benzyl-2,5-dimethyl-4-phenyl-4-piperidinol as a viscous oil with b.p. 169-178° at 2.5 mm. Four recrystallizations of this mixture from benzine (b.p. 80-100°) yielded 0.3 g of an individual isomer of 1-benzyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 94-94.5°.

Found %: N 4.75, 4.82. $C_{20}H_{25}ON$. Calculated %: N 4.75.

3 g of the oily mixture of isomers of 1-benzyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 169-178° at 2.5 mm could not be separated.

SUMMARY

The reaction of phenyllithium with 1-alkyl-2,5-dimethyl-4-piperidones (I) has been studied, and using this reaction a series of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) have been prepared and separated, in the majority of cases in the form of three spatial isomers out of the four theoretically possible. The reaction of phenyllithium with 1-cyclohexyl-2,5-dimethyl-4-piperidone and 1-phenyl-2,5-dimethyl-4-piperidone leads to the formation of only 1 stereoisomer of the corresponding phenylpiperidinol, and these reactions are consequently spatially selective, as in the case of the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones. 1-alkyl-2,5-dimethyl-4-piperidones react with Grignard reagents predominantly in the enolic form, which also explains the low yields of tertiary piperidinols obtained in this way.

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HETEROCYCLIC COMPOUNDS

44. SYNTHETIC PAIN-RELIEVING SUBSTANCES. IX. ESTERS OF 1-ALKYL-2,5-DIMETHYL-4-PHENYL-4-PIPERIDINOLS. HOMOLOGS OF PROMEDOL AND ISOPROMEDOL

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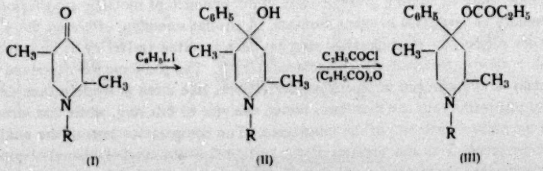
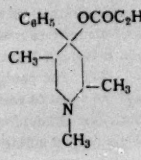
As is well known, the propionates of the two stereoisomeric β- and γ-forms of 1,2,5-trimethyl-4-phenyl-4-piperidinol (IV) exhibit extremely high pain-relieving (analgesic) activity and one of them is widely used in medicine under the name "promedol" [1]. In a continuation of systematic studies on the synthesis of and the search for new pain-relieving substances, we decided to prepare the propionates of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (III), which are the homologs of promedol and isopromedol (IV) and which differ from the latter only in the nature of the substituent on the nitrogen of the piperidine ring. A comparative pharmacological study of the propionates of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (III) enables one to examine the influence of different substituents on the nitrogen of the piperidine ring on the pain-relieving action of these compounds, which has a definite significance in establishing the connection between structure and activity in synthetic analgesics. The original 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) were prepared in the different stereoisomeric forms by the action of phenyllithium on the 1-alkyl-2,5-dimethyl-4-piperidones (I) and are described in a previous communication [2].

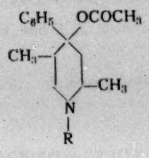


(I) (II) (III)

The propionates (III) necessary for the pharmacological studies were obtained by the action of propionyl chloride or propionic anhydride on the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) and purified as the hydrochlorides. The acetates of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinol series were also prepared for a comparison of their pain-relieving action (V).

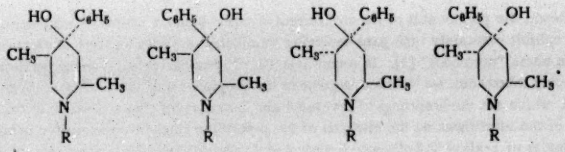


(IV)



(V)

The esterification of the stereoisomeric forms of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) depends on their spatial structure, which is illustrated by the following formulas:



The elucidation of stereochemical problems in connection with these compounds will be the subject of later communications. It should be observed that the esterification of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (II) depends not only on their spatial structure but also on the nature of the substituent on the nitrogen of the piperidine nucleus. The piperidinols indicated, with methyl groups on the nitrogen, are easily esterified by the halides even in the cold, whereas the piperidinols with higher alkyl or alicyclic radicals are esterified by the chlorides only on heating (more readily in the presence of metallic magnesium). These piperidinols cannot usually be esterified by other methods. A similar screening effect on the γ-carbonyl group by the substituent on the nitrogen of the piperidine ring has been reported earlier by us in a study of the reaction of phenyllithium with 1-alkyl-2,5-dimethyl-4-piperidones (I) [2]. The phenomenon described is explained by the fact that substituents on the nitrogen in piperidine derivatives, like those in cyclohexane derivatives, do not lie in the plane of the piperidine ring and therefore, screen one side of this ring, while the screening effect naturally depends on the nature (volume) of the substituent. The comparative tests of the analgesic activity of the hydrochlorides of the propionates and acetates of the 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (III) and (V) which were synthesized, were carried out in Prof. M. D. Mashkovsky's laboratory in the All-Union Chemical and Pharmaceutical Scientific Research Institute and the results obtained are given in the Table. The analgesic activity and toxicity of promedol are taken as unity. The toxicity of promedol is LD_{50} = 50 mg/kg (internally), the analgesic activity 2-3 times greater than that of morphine. As can be seen from the table given, the highest analgesic activity and the lowest toxicity of all the compounds studied are shown by promedol, isopromedol and α-promedol (compounds 1,2 and 3). Thus, the methyl group is the optimum substituent for analgesic and toxic properties in the propionates of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols (III). Lengthening of the alkyl chain on the nitrogen is associated not only with a lowering of the analgesic activity of the propionates by comparison with promedol, but also with a marked increase in the toxicity (approximately double). When the alkyl substituent on the nitrogen is branched, the analgesic activity of the propionates (III) almost or completely disappears (compounds 9,10,11,20). The analgesic activity of the propionates (III) also disappears completely in the case where cyclohexyl, phenyl and various alkyl substituents with functional groups (γ-alkoxypropyl, γ-dialkylaminopropyl etc.,) are situated on the nitrogen. The propionates (III) in all cases show a much greater analgesic activity than the corresponding acetates (V), and esters of other organic acids.

Spatial isomers corresponding to isopromedol (the β-forms) in all cases show a much greater analgesic activity than the corresponding γ-forms belonging to the promedol spatial series. The greatest analgesic activity is shown by the α-isomers corresponding to α-promedol, which has approximately 4 times the activity of promedol and 8-10 times the activity of morphine and is the most interesting of all well-known present-day analgesics.

Nos.	R	Isomer	Propionates (III)			Acetates	
			melting point of hydrochloride	activity	toxicity	melting point of hydrochloride	activity
1	CH_3	γ	220—221° (promedol)	1	1	219—220°	0.2
2		β	181—182 (isopromedol)	2	1	185—186	0.33
3		α	106—107 (α-promedol)	4	1		
4	C_2H_5	γ	210	0.8—1	2	212	0.1—0.2
5		β	201—202	1		182	0.3
6		α	176—177	2			
7	C_3H_7	γ	182—183	0.5	2	191	Weak
8		β	196—197	0.8—1	2	215—216	0.3
9	iso-C_3H_7	γ	145—147	0.1			
10		β	194—195	0.2			
11		α	177—178	0			
12	C_3H_5 (allyl)	γ	182—183	0.3	2	204—205	0
13		β	168—168.5	0.6—1	2	196—197	0.3
14	C_4H_9	γ	185—186	0.5		196—196.5	0.2
15		β	209—210	2	2—2.5	222—223	0.5
16	iso-C_4H_9	γ	160—161	0			
17		β	170—171	0.8—1			
18	iso-C_5H_{11}	γ	179—180	0.5			
19		β	176—177	0.8—1			
20	cyclo-C_6H_{11}		221	0		225	0
21	C_6H_5		167—168	0			
22	$C_6H_5CH_2$		193—194	0		219—220	0

EXPERIMENTAL

Propionate of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol (alpha-promedol). 60 ml propionyl chloride was added dropwise with cooling in ice to a solution of 30 g of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 106-107° in 60 ml dry dichloroethane. After two days the precipitate of hydrochlorides obtained was filtered off and recrystallized from alcohol. 5 g of the hydrochloride of the original 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 235-236° was obtained. The filtrate and the mother liquor from the recrystallization were combined, the volatile products distilled off in vacuo and the residue recrystallized from a mixture of acetone and ether. This yielded 22 g of the hydrochloride of the propionate of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 100-105°, rising to 106-107°, after repeated recrystallization from acetone.

Found %: C 62.20, 62.10; H 8.61, 8.57; N 4.87, 4.88. $C_{17}H_{25}NO_2Cl \cdot H_2O$. Calculated %: C 62.00; H 8.40; N 4.25.

The compound was obtained as the monochloride and after drying in vacuo over P_2O_5 hydrogen chloride was split off and the free propionate of 1,2,5-trimethyl-4-phenyl-4-piperidinol was obtained.

5 g of the hydrochloride of the propionate of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 106-107° was dissolved in 20 ml water and treated with an excess of concentrated ammonia. The oil which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 3 g of the free propionate of the α-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with b.p. 151-152° at 3.5 mm.

Found %: C 73.84, 73.78; H 9.07, 9.09; N 4.74, 4.67. $C_{17}H_{25}O_2N$. Calculated %: C 74.20; H 9.08; N 5.09.

Propionate of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol (isopromedol). 2 g of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 102-103° was dissolved by heating in 5 ml dichloroethane and treated with 1.5 ml propionyl chloride. After 20 minutes the solution was seeded with isopromedol and crystallization began. After 2 days, 20 ml absolute ether was added to the reaction mass. This yielded 1.7 g of isopromedol with m.p. 183-184°, which gave no melting point depression with a known sample [1].

Propionate of the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol (promedol). 2 g of the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 105-107° was dissolved by heating in 5 ml dichloroethane and treated with 1.5 ml propionyl chloride. After 25 minutes the mixture was seeded with promedol and crystallization began. After two days 20 ml absolute ether was added to the reaction mass, the precipitate was filtered off and recrystallized from a mixture of alcohol and ether. This yielded 0.8 g of promedol with m.p. 220-221°, which gave no melting point depression with a known sample [1].

Acetate of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol. 5 g of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 102-103° was dissolved by heating in 5 ml benzene and 5 ml acetyl chloride was poured into the warm solution. The reaction mass was heated until the precipitate which formed had dissolved (10-15 minutes with the acetyl chloride boiling) and left for twenty-four hours at room temperature. 40 ml absolute ether was then added to the reaction solution and the precipitate obtained filtered off and recrystallized from a mixture of acetone and ether. This yielded 2.6 g of the hydrochloride of the acetate of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with m.p. 185.5-186°.

Found %: N 4.47, 4.55. $C_{16}H_{24}O_2NCl$. Calculated %: N 4.70.

A mixture of the hydrochloride of the acetate of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol with the product of the dehydration of the β-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidinol (m.p. 191-192°) melted at 151-160°.

Propionate of the alpha isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 grams of the α-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 93-94° was dissolved in 5 ml dichloroethane (with heating) then cooled with ice and treated with 5 ml of propionyl chloride. The reaction mass was then heated for 10 hours at 65-70°, cooled to room temperature and unreacted 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol hydrochloride with m.p. 223-225° which precipitated was filtered off (0.8 g). The filtrate was evaporated in vacuo, the residue dissolved in acetone, filtered and precipitated with ether. The oil which precipitated was repeatedly recrystallized from acetone yielding 0.35 g of the hydrochloride of the propionate of the α-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m. p. 176.5-177°.

Found %: C 65.71, 65.62; H 8.63, 8.80; N 4.52, 4.67. $C_{18}H_{28}O_2NCl$. Calculated %: C 66.34; H 8.68; N 4.30.

Propionate of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol. 1 g of β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 99-100°, 2 ml benzene, 2 ml propionyl chloride and 0.2 g magnesium were heated for 6 hours until the precipitate initially formed had completely dissolved. The benzene and unreacted propionyl chloride were then distilled off in vacuo from a boiling water bath, the

residue dissolved in water, extracted with ether, treated with concentrated ammonia, extracted with ether and vacuum distilled. This yielded 0.6 g of oil with b.p. 150-155° at 5 mm, which partially crystallized on the addition of 0.6 ml of a saturated solution of hydrogen chloride in alcohol. Recrystallization of the resultant precipitate from a mixture of acetone and ether yielded 0.3 g of the hydrochloride of the propionate of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 201.5-202.5°.

Found %: C 66.20, 66.29; H 8.70, 8.52; N 4.47, 4.62. $C_{18}H_{28}O_2NCl$. Calculated %: C 66.36; H 8.67; N 4.30.

Propionate of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5.12 g of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 101-101.5°, 13.4 g propionic anhydride and 9.8 g dry pyridine were heated for 5 hours at 160-170°. The pyridine, propionic acid and unreacted propionic anhydride were then distilled off in vacuo. The residue was dissolved in water, saturated with sodium carbonate, the reaction product extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 5.4 g of the propionate with b.p. 127.5-132° at 1.5 mm, which was converted to the hydrochloride in the usual way. After 3 recrystallizations from a mixture of alcohol and ether, 3 g of the hydrochloride of the propionate of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 210° was obtained.

Found %: N 4.84, 4.72; Cl 11.32, 11.27. $C_{18}H_{28}O_2NCl$. Calculated %: N 4.30; Cl 11.92.

Reaction of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with propionyl chloride in the cold. 2 g of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 99-100° in 5 ml dichloroethane was treated with 1.5 ml propionyl chloride. After standing for two days at room temperature 1.8 g of the hydrochloride of the original alcohol with m.p. 215-217° was precipitated.

Reaction of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with propionyl chloride in the cold. 2 g of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 104.5-105° in 5 ml dichloroethane was treated with 1.5 ml propionyl chloride. After two days 2 g of the hydrochloride of the original alcohol with m.p. 190-191° was precipitated, and a mixture of this substance and the hydrochloride of the propionate of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 210°) melted at 162-165°.

Acetate of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol. 3.4 g of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 99-100°, 20 ml dry xylene, 7 ml acetyl chloride and 0.4 g magnesium turnings were heated for 7 hours at 100-105°. The xylene and unreacted acetyl chloride were then distilled off in vacuo. The residue was treated with ether, dissolved in water, saturated with sodium carbonate, and the base which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 2.6 g of the acetate with b.p. 136.5-141° at 3 mm, which was converted to the hydrochloride in the usual way. After two recrystallizations from a mixture of alcohol and ether 1.2 g of the hydrochloride of the acetate of the β-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 182° was obtained.

Found %: N 5.01, 4.99; Cl 11.09, 11.17. $C_{17}H_{26}O_2NCl$. Calculated %: N 4.49; Cl 11.39.

Acetate of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5 g of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 101-101.5°, 15 ml benzene, 0.5 g magnesium turnings and 10 ml acetyl chloride were heated for 10 hours at 70-75°. The magnesium was then filtered off and the benzene and unreacted acetyl chloride distilled off in vacuo. The residue was treated with ether, dissolved in water, saturated with sodium carbonate, the product extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 3.6 g of the acetate with b.p. 131-135° at 1.5 mm, which was converted to the hydrochloride in the usual way. After recrystallization from a mixture of alcohol and ether, 3.1 g of the hydrochloride of the acetate of the γ-isomer of 1-ethyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 212° was obtained.

Found %: N 4.54, 4.67; Cl 11.34, 11.41. $C_{17}H_{26}O_2NCl$. Calculated %: N 4.49; Cl 11.39.

Propionate of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. 0.5 g magnesium turnings and 10 ml propionyl chloride were added to a solution of 5 g of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 53.5-55°) in 5 ml benzene. The reaction mass rapidly boiled and a voluminous precipitate appeared in the flask. When the evolution of heat had ceased, the reaction mass was heated for 10 hours at 100-105° until the precipitate initially formed had completely dissolved. When heating had finished, the benzene and excess propionyl chloride were distilled off in vacuo, the residue treated with absolute ether and dissolved in water. The aqueous solution was saturated with Na_2CO_3, the product extracted with ether, dried with Na_2SO_4 and vacuum distilled: 1st fraction, b. p. 130-137° at 2.5 mm, 0.2 g; 2nd, b. p. 137-145° at 2.5 mm, 4.5 g; residue 1.5 g. The 2nd fraction was converted in the usual way to the hydrochloride, and after two recrystallizations of the latter from alcohol and ether 3 g of the hydrochloride of the propionate of the β-isomer with m. p. 196-197° was obtained.

Found %: Cl 10.10, 10.32. $C_{19}H_{30}O_2NCl$. Calculated %: Cl 10.50.

Propionate of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5 g of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°), 10 ml benzene, 15 ml propionyl chloride and 0.5 g magnesium were heated for 10 hours on a boiling water bath. The benzene and excess propionyl chloride were then distilled off in vacuo, the residue dissolved in water, extracted with ether, treated with concentrated ammonia (20 ml), the product extracted with ether, dried with sodium sulfate and vacuum distilled: 1st fraction, b.p. 104-130° at 2.5 mm, 0.5 g; 2nd fraction, b.p. 135-145° at 2.5 mm, 5.2 g. Residue in distillation flask 0.3 g.

The 2nd fraction was converted to the hydrochloride in the usual way, and on recrystallization of the product from alcohol and ether 3.5 g of the hydrochloride of the propionate of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 182-183° was obtained.

Found %: N 4.49, 4.66; Cl 10.40, 10.40. $C_{19}H_{30}O_2NCl$. Calculated %: N 4.13; Cl 10.50.

Acetate of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. 0.5 g of magnesium turnings and 10 ml acetyl chloride were added to a solution of 5 g of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 53.5-55°) in 10 ml benzene. The mixture rapidly became hot, began to boil, and a considerable quantity of a colorless precipitate separated. The reaction mass was heated for 7.5 hours until the precipitate which had formed initially had completely dissolved. When the heating had finished, the benzene and excess acetyl chloride were distilled off in vacuo, the residue treated with 10 ml concentrated ammonia, the product extracted with ether, dried with sodium sulfate and vacuum distilled; 1st fraction, b.p. 120-133° at 2.5 mm, 0.2 g; 2nd fraction, b.p. 134-137° at 2.5 mm, 4.0 g. Residue in distillation flask 1.5 g.

The 2nd fraction was converted to the hydrochloride in the usual way. After two recrystallizations of the product from alcohol 2.5 g of the hydrochloride of the acetate of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 215-216° was obtained.

Found %: N 4.70, 4.55; Cl 10.92, 10.70. $C_{18}H_{28}O_2NCl$. Calculated %: N 4.30; Cl 10.90.

Acetate of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. a) 10 g of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°), 20 ml acetyl chloride, 20 ml benzene and 0.5 g magnesium turnings were heated at 70-75° for 11 hours. The benzene and unreacted acetyl chloride were distilled off under reduced pressure at the water pump. The residue was dissolved in water (50 ml), extracted with ether, treated with 10 ml concentrated ammonia, the oil which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 8.2 g of the acetate in the form of a thick oil with b.p. 143-145° at 3 mm. Residue in the distillation flask 2.8 g. The material obtained was dissolved in 50 ml absolute ether and saturated with dry hydrogen chloride. After two recrystallizations of the precipitate obtained from a mixture of alcohol and ether 5.5 g of the hydrochloride of the acetate of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol, with m.p. 191-191.5° was obtained.

Found %: N 4.31, 4.50; Cl 10.85, 10.75. $C_{19}H_{28}O_2NCl$. Calculated %: N 4.30; Cl 10.90.

b) 5 g of the γ-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°), 10 ml acetic anhydride and 10 ml pyridine were heated in a metal ampoule for 7 hours at 158-162°. The pyridine and acetic anhydride were then distilled off in vacuo, the residue dissolved in 50 ml ether and saturated with dry hydrogen chloride. The precipitate obtained was recrystallized three times from a mixture of alcohol and ether, as a result of which 2.5 g of the hydrochloride of the acetate of the γ-isomer of 1-propyl-2, 5-dimethyl-4-phenyl-4-piperidinol with m.p. 191-192° was obtained and this gave no depression of the melting point when mixed with the sample described above.

The reaction of acetyl chloride on the lithium alkoxide of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol. 22.5 g 1-propyl-2,5-dimethyl-4-piperidone in 40 ml absolute ether was added with cooling by a mixture of ice and salt (-10°) over a period of 1 hour to a solution of phenyllithium prepared from 2.3 g metallic lithium and 25 g bromobenzene in 120 ml absolute ether. On the next day a solution of 23 g acetyl chloride in 50 ml absolute ether was added with cooling by ice water. The reaction mass was heated for 5 hours with the ether boiling and treated with water (100 ml). The ether and water layers were separated and the middle layer of oil gradually crystallized. After recrystallization from alcohol 23 g of a mixture of the hydrochlorides of the isomeric acetates of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinols with m.p. 155-185° was obtained, consisting for the most part of the γ-isomer.

Found %: N 4.43, 4.21; Cl 10.45, 10.67. $C_{18}H_{28}ONCl$. Calculated %: N 4.30; Cl 10.90.

The aqueous solution and the mother liquors from the recrystallization yielded 1.7 g of the hydrochloride of the β-isomer of 1-propyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 201.5-202° described earlier [2], and this did not give a melting point depression with a known specimen.

Propionate of the α-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol. 3 g of the α-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 63-65° was dissolved in 6 ml dichloroethane and treated with 6 ml propionyl chloride with cooling by ice. A voluminous crystalline precipitate was obtained. The reaction mixture was then heated for 10 hours at 55-65°, cooled, the hydrochloride of the unreacted alcohol filtered off (2.5 g with m.p. 230-235°), the filtrate evaporated in vacuo and treated with 20 ml absolute ether. The precipitate obtained was filtered off and recrystallized twice from acetone. This yielded 0.55 g of the hydrochloride of the propionate of the α-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 110-114°. After three days drying at 50° in vacuo over P_2O_5, m.p. 177-178°.

Found %: C 66.41, 66.35; H 9.02, 9.11; N 3.78, 3.73. $C_{19}H_{30}O_2NCl$. Calculated %: C 67.13; H 8.90; N 4.13.

Propionate of the β-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the β-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 67-69°), 5 ml benzene, 5 ml propionyl chloride and 0.5 g magnesium were stirred for 10 hours at 90-100°. The benzene and unreacted propionyl chloride were then distilled off in vacuo, the residue dissolved in dilute hydrochloric acid (1:1), extracted with ether, treated with ammonia, and the base which separated extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 1.5 g of the propionate of the β-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol, the hydrochloride of which melted at 194-195° after two recrystallizations from a mixture of alcohol and ether.

Found %: N 4.34, 4.30. $C_{19}H_{30}O_2NCl$. Calculated %: N 4.13.

Propionate of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5 g of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 103-104°), 10 ml benzene, 10 ml propionyl chloride and 0.5 g magnesium were stirred for 10 hours at 80-90°. After treatment similar to that described in the preceding experiment, 5.3 g of the propionate of the γ-isomer of 1-isopropyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 135-145° at 4 mm was obtained, and the hydrochloride of this substance melted at 145-147° (from a mixture of alcohol and ether).

Found %: N 4.27, 3.92. $C_{19}H_{30}O_2NCl$. Calculated %: N 4.13.

Propionate of the β-isomer of 1-allyl-2,5-dimethyl-3-phenyl-4-piperidinol. 5 g of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 73-75°), 10 ml benzene, 10 ml propionyl chloride and 0.5 g magnesium turnings were heated for 10 hours at 100-105°. The benzene and excess propionyl chloride were then distilled off in vacuo. The residue was dissolved in water, extracted with ether, saturated with sodium carbonate, the free base extracted with ether, dried with sodium sulfate and vacuum distilled: 1st fraction, b.p. 130-140° at 2.5 mm, 0.2 g; 2nd fraction, b.p. 141-142° at 2.5 mm, 4 g. Residue in distillation flask 0. 5 g.

The 2nd fraction was converted to the hydrochloride in the usual way. Recrystallization of this material from a mixture of alcohol and ether yielded 2.6 g of the hydrochloride of the propionate of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 168-168.5°.

Found %: N 4.17, 4.38; Cl 10.42, 10.32. $C_{19}H_{28}O_2NCl$. Calculated %: N 4.16; Cl 10.52.

Propionate of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5 g of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°), 10 ml benzene, 10 ml propionyl chloride and 0.5 g magnesium were heated at 90-95° for 10 hours. After treatment similar to that described in the previous experiment 5 g of the propionate with b.p. 149-151° at 3 mm was obtained and converted to the hydrochloride in the usual way. Recrystallization of this material from a mixture of alcohol and ether yielded 2.5 g of the hydrochloride (of the propionate) of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 181-183°.

Found %: Cl 10.38, 10.88. $C_{19}H_{28}O_2NCl$. Calculated %: Cl 10.52.

Acetate of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol. 0.2 g of magnesium turnings and four ml of acetyl chloride were added to a solution of 2 g of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol in 5 ml benzene. When evolution of heat had ceased the reaction mass was heated for 5 hours at 80-90° until the precipitate obtained had completely dissolved. When the heating had finished the benzene and unreacted acetyl chloride were distilled off in vacuo, the residue dissolved in water, extracted with ether and saturated with sodium carbonate. The base which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 1.4 g of the acetate with b.p. 133-145° at 2.5 mm, which was converted to the hydrochloride in the usual way. After two recrystallizations of this substance from a mixture of alcohol and ether 0.5 g of the hydrochloride of the acetate of the β-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 196-197° was separated.

Found %: N 4.64, 4.54; Cl 10.88, 11.00. $C_{18}H_{26}O_2NCl$. Calculated %: N 4.33; Cl 11.00.

Acetate of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol. 3 g of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 93-94°), 6 ml benzene, 6 ml acetyl chloride and 0.2 g magnesium turnings were heated at 85-90° for 10 hours. The reaction mass was treated in a similar way to that in the previous experiment, as a result of which 2.2 g of the acetate with b.p. 137-141° at 2.5 mm was obtained, dissolved in 20 ml absolute ether and saturated with dry hydrogen chloride. The precipitate obtained was recrystallized twice from a mixture of alcohol and ether, yielding 1.2 g of the hydrochloride of the acetate of the γ-isomer of 1-allyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 204-205°.

Found %: N 4.76, 4.70; Cl 11.10, 11.20. $C_{18}H_{26}O_2NCl$. Calculated %: N 4.33, Cl 11.00.

Propionate of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 66-68°), 5 ml benzene, 5 ml propionyl chloride and 0.4 g magnesium were stirred for 4 hours at 90-95°. The precipitate which formed on mixing the reagents dissolved completely after heating for 2 hours. The benzene and unreacted propionyl chloride were distilled off in vacuo, the residue dissolved in dilute hydrochloric acid (1:1), extracted with ether, treated with ammonia, the base which separated was extracted with ether, dried with sodium sulfate and vacuum distilled.

This yielded 2 g of the propionate of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 152-158° at 3 mm, which formed a hydrochloride melting at 209-210° (from a mixture of alcohol and ether).

Found %: N 3.80, 3.87. $C_{26}H_{33}O_2NCl$. Calculated %: N 3.96.

Propionate of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 95-96°), 5 ml benzene, 5 ml propionyl chloride and 0.5 g magnesium were stirred at 90-100° for 8 hours. The benzene and unreacted propionyl chloride were then distilled off in vacuo. The residue was dissolved in water, extracted with ether, treated with ammonia, the base which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 1.5 g of the propionate of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 130-140° at 2 mm, which formed a hydrochloride with m.p. 185-186°.

Found %: N 3.84, 3.92. $C_{26}H_{33}O_2NCl$. Calculated %: N 3.96.

Acetate of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 71-72°), 5 ml acetyl chloride, 5 ml benzene and 0.5 g magnesium were stirred for 6 hours at 80-90°. The benzene and acetyl chloride were then distilled off in vacuo. The residue was treated with ether and recrystallized three times from a mixture of alcohol and ether. This yielded 2 g of the hydrochloride of the acetate of the β-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 222-223°.

Found %: N 3.91, 4.06. $C_{25}H_{36}O_2NCl$. Calculated %: N 4.13.

Acetate of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 95-96°), 5 ml benzene, 5 ml acetyl chloride and 0.4 g magnesium were heated at 90-95° for 8 hours. The residue remaining after distillation of the benzene and acetyl chloride was dissolved in water, extracted with ether and treated with ammonia. The oil which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 2 g of the acetate of the γ-isomer of 1-butyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 140-150° at 3 mm, which formed a hydrochloride which melted at 196-196.5° (from a mixture of alcohol and ether).

Found %: N 3.94, 4.13. $C_{25}H_{36}O_2NCl$. Calculated %: N 4.13.

Propionate of the β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 29-30°), 5 ml benzene, 5 ml propionyl chloride and 0.4 g magnesium were stirred at 90-95° for 6 hours. The benzene and unreacted propionyl chloride were then distilled off in vacuo, the residue dissolved in dilute hydrochloric acid (1:1), extracted with ether, treated with ammonia, the base extracted with ether, dried with ignited sodium sulfate and vacuum distilled. This yielded 2 g of the propionate of the β-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 135-140° at 2 mm, which formed a hydrochloride with m.p. 170-171° after 2 recrystallizations from a mixture of alcohol and ether.

Found %: N 4.06, 3.88. $C_{26}H_{32}O_2NCl$. Calculated %: N 3.96.

Propionate of the γ-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the γ-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 71-73°), 2.5 ml benzene, 2.5 ml propionyl chloride and 0.4 g magnesium were stirred for 4 hours at 90-95°. After the treatment described in the previous experiment 2 g of the propionate of the γ-isomer of 1-isobutyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 140-150° at 2.5 mm was obtained, giving a hydrochloride which melted at 160-161° (from a mixture of alcohol and ether).

Found %: N 4.19, 4.03. $C_{26}H_{32}O_2NCl$. Calculated %: N 3.96.

Propionate of the β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol. 2.5 g of the β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 80-82°), 2.5 ml propionyl chloride, 2.5 ml benzene and 0.4 g magnesium were heated for 5 hours at 80-95°. The residue remaining after the distillation of the benzene and the unreacted propionyl chloride was dissolved in water, extracted with ether, and treated with ammonia. The base which separated was extracted with ether, dried with sodium sulfate and vacuum distilled. This yielded 2 g of the propionate of the β-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 155-162° at 3 mm, which formed a hydrochloride with m.p. 176-177° after 3 recrystallizations from a mixture of alcohol and ether.

Found %: N 3.56, 3.78. $C_{21}H_{34}O_2NCl$. Calculated %: N 3.82.

Propionate of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol. a) A mixture of 1 g of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 109-110°) and 1 ml propionyl chloride was heated at 50-60° for 10 minutes and left to stand for 3 weeks at room temperature. The propionyl chloride was then distilled off in vacuo, the residue dissolved in water, extracted with ether, treated with ammonia, the base which separated extracted with ether, dried with sodium sulfate and saturated with dry hydrogen chloride. The oil which separated crystallized after reprecipitation from alcohol and ether. Repeated recrystallization from a mixture of alcohol and ether yielded 0.2 g of the hydrochloride of the propionate of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with m. p. 179-180°.

Found %: N 3.92, 3.83. $C_{21}H_{34}O_2NCl$. Calculated %: N 3.81.

Esterification of the γ- and β-isomers of 1,2,5-trimethyl-4-phenyl-4-piperidinol with propionyl chloride under analogous conditions gave the corresponding propionates (promedol and isopromedol) in 80-90% yield.

b) 2.5 g of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 109-110°), 2.5 ml propionyl chloride, 2.5 ml benzene and 0.4 g magnesium were heated for 5 hours at 85-95°. The benzene and propionyl chloride were then distilled off in vacuo. The residue was dissolved in water, extracted with ether, treated with ammonia, the base extracted with ether, dried with ignited sodium sulfate and vacuum distilled. This yielded 1.2 g of the propionate of the γ-isomer of 1-isoamyl-2,5-dimethyl-4-phenyl-4-piperidinol with b.p. 145-155° at 3 mm, which formed a hydrochloride melting at 179-180° and giving no melting point depression when mixed with the specimen obtained in the previous experiment.

Propionate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol. 10 g of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol with melting point 114.5-115°, 20 ml benzene, 20 ml propionyl chloride and 0.5 g magnesium turnings were heated for 11 hours at 90-100° until the precipitate initially formed had completely dissolved. The benzene and unreacted propionyl chloride were then distilled off in vacuo. The residue was treated with ether and recrystallized from water and then from a mixture of alcohol and ether. This yielded 6.6 g of the hydrochloride of the propionate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 220.5-221.5°.

Found %: Cl 9.73, 9.31. $C_{22}H_{34}O_2NCl$. Calculated %: Cl 9.37.

The mother liquor was saturated with sodium carbonate, extracted with ether and dried with sodium sulfate. After distillation of the ether and recrystallization of the residue from benzine (b.p. 80-100°) 2.6 g of the free propionate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol, contaminated with original piperidinol, was obtained, m.p. 85-92°.

Acetate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol. 5 g 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol (m.p. 114.5-115°), 10 ml benzene, 10 ml acetyl chloride and 0.2 g magnesium turnings were heated for 13 hours at 70-80° until the precipitate initially formed had completely dissolved. The benzene and unreacted acetyl chloride were then distilled off in vacuo, the residue treated with ether and recrystallized from water and then from alcohol. This yielded 3.7 g of the hydrochloride of the acetate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 224.5-225°.

Found %: N 4.01, 3.77; Cl 9.20, 9.05. $C_{21}H_{32}O_2NCl$. Calculated %: N 3.85; Cl 9.75.

The aqueous mother liquor was saturated with sodium carbonate, extracted with ether and dried with sodium sulfate. After distillation of the ether and recrystallization from benzine, 1.3 g of the free acetate of 1-cyclohexyl-2,5-dimethyl-4-phenyl-4-piperidinol with m.p. 106-108° was obtained.

Found %: N 4.56, 4.39. $C_{21}H_{31}O_2N$. Calculated %: N 4.25.

SUMMARY

The propionates of a series of stereoisomeric 1-alkyl-2,5-dimethyl-4-piperidinols, homologs of promedol and isopromedol, have been synthesized. By comparison with the latter, the esters obtained show greater toxicity and reduced pain-relieving (analgesic) activity, while certain propionates, containing branched and cyclic radicals (isopropyl, cyclohexyl) on the nitrogen atom, have almost no analgesic activity. Thus, these compounds are better analgesics when the group on the nitrogen atom is the methyl group.

The acetates of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols in all cases show less analgesic activity than the corresponding propionates. The β-isomers (of the isopromedol type) in all cases show 2-3 times greater analgesic activity than the corresponding γ-isomers (of the promedol type). It has been shown that the esterification of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidinols depends to a great extent on the spatial structure and also on the nature of the substituent on the nitrogen of the piperidine ring.

LITERATURE CTIED

[1] L. N. Nazarov et al., J. Gen. Chem. 26, 2798 (1956).*

[2] L. N. Nazarov et al., J. Gen. Chem. 26, 3157 (1956).*

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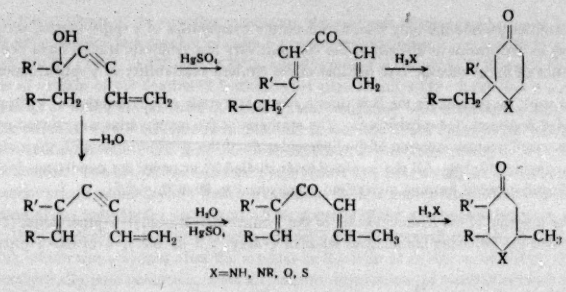
* Original Russian pagination. See C. B. Translation.

HETEROCYCLIC COMPOUNDS

45. CYANHYDRINS OF γ-PIPERIDONES, TETRAHYDRO-γ-PYRONES AND TETRAHYDRO-γ-THIOPYRONES. STEREOCHEMISTRY OF THE CYANHYDRIN SYNTHESIS

I. N. Nazarov and B. V. Unkovsky

Some years ago, new simple methods were worked out in our laboratory for the synthesis of different γ-piperidones, tetrahydro-γ-pyrones and tetrahydro-γ-thiopyrones by the reaction of ammonia, primary amines, water and hydrogen sulfide with divinyl ketones obtained by the hydration of divinylacetylenic hydrocarbons in aqueous methanol solutions [1-3] or by the isomerization of vinylethinylcarbinols [4,5].



The high reactivity of the dienones, the ease of converting them into heterocyclic γ-ketones and the availability of the starting materials revealed great possibilities for the synthesis of countless new physiologically active compounds.

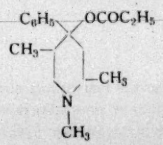
Particular interest is attached to the method described above for preparing different γ-piperidones with varying substituents in the piperidine nucleus, in view of the fact that these compounds are the starting materials for the synthesis of the structural analogs of the alkaloids of the tropane and morphine group, and these analogs have similar pain-relieving, anesthetic and spasmolytic action to tropane and morphine themselves.

In recent years a detailed study has been made in our laboratory of the various reactions of γ-piperidones, with a view to finding new physiologically active compounds and clarifying the relationship between their activity and chemical structure [6-8]. Starting from γ-piperidones we synthesized, in particular, highly effective synthetic pain-relieving substances belonging to the series of esters of 4-phenyl-4-piperidinols, whose activity is several times greater than that of morphine. One of the most interesting of the synthetic analgesics is promedol (the propionate of 1,2,5-trimethyl-4-phenyl-4-piperidinol), which was prepared in our laboratory [6].

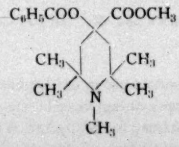
In connection with the importance of γ-piperidones in the synthesis of new anesthetic and analgesic substances, it became of interest to examine their reaction with hydrogen cyanide and study the conversion of the cyanhydrins formed in this reaction into the corresponding piperidine analogs of cocaine having structures of the α-eucaine and α-cocaine type.

The synthesis of α-eucaine was achieved as early as 1896 [9a], starting from the cyanhydrin of the only γ-piperidone known at that time – triacetonamine. Some time later the cyanhydrin of tropinone was obtained by the reaction of hydrogen cyanide and tropinone, and converted in similar fashion into the structural isomer of cocaine – α-cocaine [10].

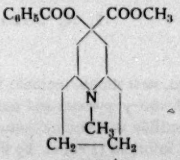
There are reports in the patent literature of the preparation of the cyanhydrins of vinyl-and benzaldiacetonamines [11], several of their homologs, and also of the cyanhydrin of 1-methyl-4-piperidone [12].



promedol



α-eucaine

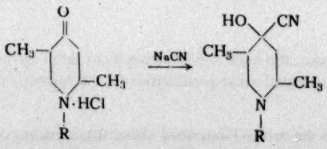


α-cocaine

These few examples provide the only information on the cyanhydrins of γ-piperidones, which have been very little studied up to the present as a result of the fact that very few synthetic studies have been made in the field of anesthetics of the α-eucaine type because of the limited availability of γ-piperidones.

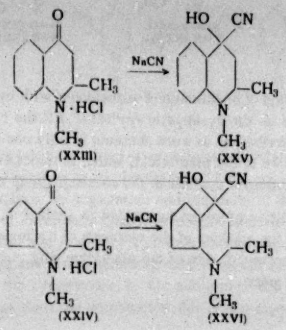
In the present work we present for the first time a systematic study of the reaction of hydrogen cyanide with various 1-alkyl-2,5-dimethyl-4-piperidones. The synthesis of the cyanhydrins was carried out by the reaction of a concentrated aqueous solution of the hydrochloride of the γ-piperidone with the calculated quantity of sodium cyanide [10-13]. All the γ-piperidones studied by us under the conditions described reacted vigorously with hydrogen cyanide forming crystalline cyanhydrins in 80-97% yield.

In this way the reaction of the hydrochlorides of the 1-alkyl-2,5-dimethyl-4-piperidones (I-XI) with sodium cyanide yielded the following homologous series of 1-alkyl-2,5-dimethyl-4-cyano-4-piperidinols (XII–XXII):



R = H (I),
R = CH_3 (II),
R = C_2H_5 (III),
R = C_3H_7 (IV),
R = iso-C_3H_7 (V),
R = C_3H_5 (VI),
R = C_4H_9 (VII),
R = iso-C_4H_9 (VIII),
R = iso-C_5H_{11} (IX),
R = cyclo-C_6H_{11} (X),
R = C_6H_5 (XI),
R = H (XII),
R = CH_3 (XIII),
R = C_2H_5 (XIV),
R = C_3H_7 (XV),
R = iso-C_3H_7 (XVI),
R = C_3H_5 (XVII),
R = C_4H_9 (XVIII),
R = iso-C_4H_9 (XIX),
R = iso-C_5H_{11} (XX),
R = cyclo-C_6H_{11} (XXI),
R = C_6H_5 (XXII).

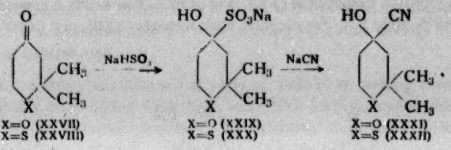
In a similar way, the crystalline cyanhydrins (XXV) and (XXVI), containing a condensed piperidine nucleus, were obtained in 96-97% yield from the dicyclic aminoketones (XXIII) and (XXIV).



In spite of the mildness of the reaction conditions, the synthesis of the cyanhydrins of 1-alkyl-2,5-dimethyl-4-piperidones is accompanied in a number of cases by condensation processes, especially in the preparation of the cyanhydrins (XII), (XIV), (XXII) and (XXVI), and this makes purification of these compounds difficult. The cyanhydrins of certain of the 1-alkyl-2,5-dimethyl-4-piperidones (XIV–XXI) show a tendency to undergo solvation, as a result of which the products obtained by recrystallizing these substances from benzene or ethyl acetate are obtained as the solvated forms, but only in the case of the cyanhydrins (XIV), (XVI) and (XX) do these forms prove relatively stable and they then lose solvent of crystallization only after prolonged drying in a vacuum desiccator. The crystalline solvated cyanhydrins (XV) and (XVIII) are obtained as large well formed deliquescent prisms which rapidly form a transparent oil and then crystallize only slowly in a desiccator with the formation of the individual cyanhydrins. This property of the cyanhydrins led us in a number of cases to use the crystalline products for further reactions without preliminary purification by recrystallization. The cyanhydrin (XIX), which was obtained after the reaction in the form of an oil, could not be purified and isolated in an analytically pure condition, since on vacuum distillation (at residual pressure between 2 and 10 mm) it readily split off the elements of hydrogen cyanide and gave the original γ-piperidone (VIII) in quantitative yield. Similar ease of removal of hydrogen cyanide has been noted in the literature for other cyanhydrins [14].

Together with the synthesis of the cyanhydrins of γ-piperidones, it seemed of interest to us to study the reaction of hydrogen cyanide with certain other heterocyclic γ-ketones: the tetrahydro-γ-pyrones and tetrahydro-γ-thiopyrones, which have recently become readily available as a result of work done in our laboratory [4,5].

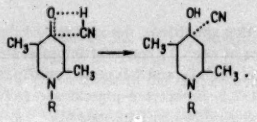
The addition of 40% sodium bisulfite solution to aqueous solutions of 2,2-dimethyltetrahydropyran-4-one (XXVII) and 2,2-dimethyltetrahydrothiopyran-4-one (XXVIII) leads readily to the formation of the corresponding bisulfite compounds (XXIX) and (XXX), which are easily converted, by the action of concentrated aqueous sodium cyanide solution, into the crystalline cyanhydrins (XXXI) and (XXXII) in yields of 70 and 83% respectively:



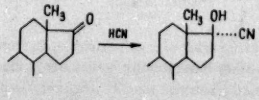
X=O (XXVII) X=S (XXVIII) X=O (XXIX) X=S (XXX) X=O (XXXI) X=S (XXXII)

The study of the reaction of 1-alkyl-2,5-dimethyl-4-piperidones with hydrogen cyanide has revealed interesting stereochemical peculiarities in the cyanhydrin synthesis. All the cyanhydrins of 1-alkyl-2,5-dimethyl-4-piperidones (XII–XXII) described by us were obtained in only one of the four theoretically possible stereoisomeric forms, in yields often close to the theoretical, which provides evidence for the spatially selective character of the addition of hydrogen cyanide to the carbonyl group in these *a*-substituted ketones.

The spatial directivity of the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones can be easily explained by postulating that the addition of the elements of hydrogen cyanide to the carbonyl group takes place from the more exposed (unscreened) side of the piperidine ring, i.e., from the opposite side to the methyl group neighboring the carbonyl group:



The addition of hydrogen cyanide and acetylene to *a*-substituted ketones of the carbocyclic series takes place in exactly the same way; with 17-ketosteroids, for example, rupture of the double bond of the carbonyl group is possible only when the reagent being added approaches from the *a*-side, i.e, from the unscreened side opposite to the angular methyl group.

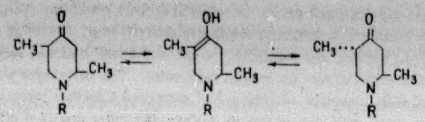


The reaction of certain other cyclic ketones, for example, camphenilone [18] and *a*-substituted cyclohexanones [19] with organometallic compounds takes place in similar fashion.

Thus, we have shown that the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones has a clearly defined spatially directive character and that these γ-piperidones, under the conditions of the cyanhydrin synthesis, react in only one stereoisomeric form.

The formation of three of the four theoretically possible spatial isomers in other addition reactions to the carbonyl group in 1-alkyl-2,5-dimethyl-4-piperidones which take place in alkaline medium [6,7] may

be explained by the reversible isomerization of these piperidones under the influence of alkaline enolizing agents, which takes place similarly to the isomerization of the carbocyclic ketones [20-22].



Among the reactions of 1-alkyl-2,5-dimethyl-4-piperidones involving the reversible cis-trans isomerization referred to above and leading to the formation of three out of four theoretically possible stereoisomers, are included the catalytic hydrogenation and reduction of the carbonyl group [7], and the condensations under the influence of alkaline reagents with acetylene, vinylacetylene and organolithium compounds [6,7]. At the same time there is usually a predominating proportion of one spatial isomer, which, as we assume, contains the hydroxyl and the neighboring methyl groups in the cis-position relative to one another and is formed, in a similar way to the cyanhydrins, by the addition of the reagent to the carbonyl group of the 1-alkyl-2,5-dimethyl-4-piperidones from the unprotected side of the piperidone ring opposite to the neighboring methyl group.

EXPERIMENTAL

2,5-Dimethyl-4-cyano-4-piperidinol (XII). A solution of 29.4 g sodium cyanide in 50 ml water was added dropwise with cooling by ice and uninterrupted stirring over a period of 1 hour to a solution of 44.6 g freshly distilled 2,5-dimethyl-4-piperidone (I) (b.p. 64-66° at 4 mm, n_D^{20} 1.4665) [1] in 150 ml 15% hydrochloric acid. After the addition of the sodium cyanide the stirring was continued for 2 hours at room temperature The precipitate obtained was filtered off, washed twice with ice water and dried in a vacuum desiccator. 26.1 g of cyanhydrin (XII) was obtained as snow-white crystals melting at 101-104°. M. p. 103.5-104° after recrystallization from ethyl acetate.

Found %: N 17.89, 17.87. $C_8H_{14}ON_2$. Calculated %: N 18.18.

The aqueous solution, which had a weakly alkaline reaction, was saturated with potassium carbonate, the oil which rose to the surface was extracted five times with ether, and the combined ether extracts dried with ignited sodium sulfate. After distillation of the ether the residue crystallized rapidly. When this had been washed with ether a further 20 g of cyanhydrin was obtained. The experiment described yielded in all 46.1 g (85%) of cyanhydrin (XII). The other cyanhydrins described below were obtained under similar conditions.

1,2,5-trimethyl-4-cyano-4-piperidinol (XIII). A solution of 29.4 g sodium cyanide in 50 ml water was added to a solution of 56.4 g freshly distilled 1,2,5-trimethyl-4-piperidinol (II) (b.p. 56-57° at 3 mm, n_D^{20} 1.4600) [1] in 150 ml 15% hydrochloric acid. After the addition of the sodium cyanide, stirring was continued for 1 hour at room temperature. The precipitate obtained was filtered off, washed twice with ice water and dried in a vacuum desiccator. 58.9 g of cyanhydrin was obtained as a colorless crystalline material melting at 125-129°. After recrystallization from ethyl acetate 56.0 g of large prismatic crystals with m.p. 128-129° was obtained.

Found %: N 16.70, 16.66. $C_9H_{16}ON_2$. Calculated %: N 16.66.

The weakly alkaline filtrate was saturated with potassium carbonate and the oil which rose to the surface was extracted four times with ether and the ether extracts dried with ignited sodium sulfate. The oily residue from the ether distillation soon crystallized. A further 6.6 g of cyanhydrin identical with the main product was obtained. In all, 65.5 g (97.2%) of cyanhydrin (XIII) was obtained.

1-Ethyl-2,5-dimethyl-4-cyano-4-piperidinol (XIV). A solution of 14.7 g sodium cyanide in 20 ml water was added to a solution of 15.5 g 1-ethyl-2,5-dimethyl-4-piperidone (III) (b.p. 76-78° at 6 mm, n_D^{20} 1.4630) [3] in 75 ml 15% hydrochloric acid. Stirring was continued for one and a half hours at room temperature, and then stopped, since the product began to turn an intense dark color. The oily layer was extracted with ether, the aqueous layer saturated with potassium carbonate and extracted a further three times with ether. The combined ether extracts were dried with ignited sodium sulfate, the ether distilled off and the residue rapidly crystallized. This yielded 16.9 g of cyanhydrin (XIV), which after recrystallization from benzine (b.p. 80-100°) had the form of gleaming star-shaped clusters, and from ethyl acetate the form of large rhombic crystals. When the crystals were dried for several hours in a vacuum desiccator they lost their luster and transparency and afterwards 15.1 g of cyanhydrin (XIV) melting at 98-99° was obtained.

Found %: N 15.48, 15.52. $C_{10}H_{18}ON_2$. Calculated %: N 15.38.

A small quantity of less pure material continued to precipitate from the mother liquor.

1-Propyl-2,5-dimethyl-4-cyano-4-piperidinol (XV). A solution of 29.4 g sodium cyanide in 50 ml water was added to a solution of 40.0 g 1-propyl-2,5-dimethyl-4-piperidone (IV) (b.p. 88-89° at 8 mm, n_D^{20} 1.4602), [3] in 150 ml 15% hydrochloric acid. After addition of the sodium cyanide stirring was continued for one and a half hours at room temperature. The oily product was extracted with ether, the aqueous solution saturated with potassium carbonate and also extracted three times with ether, and the combined ether extracts dried with sodium sulfate. The residue left in the form of an opalescent oil after the distillation of the ether slowly crystallized. In the subsequent experiments crystallization was achieved rapidly by seeding with pure cyanhydrin. 44.5 g of cyanhydrin (XV) was obtained, which after 2 recrystallizations from benzine or ethyl acetate formed large colorless prismatic crystals, rapidly liquefying in the desiccator (over calcium chloride) to a transparent oil, which then crystallized slowly to a snow-white mass.

38.4 g of cyanhydrin (XV) was separated, melting at 93-94°.

Found %: N 13.94, 14.03. $C_{11}H_{20}ON_2$. Calculated %: N 14.28.

Methiodide – large clusters, melting at 172-174° (decomp.) after recrystallization from alcohol.

Found %: N 8.18, 7.99. $C_{12}H_{23}ON_2I$. Calculated %: N 8.27.

Less pure crystals slowly precipitated from the mother liquors from the cyanhydrin recrystallizations. An attempt to concentrate the solution led to the formation of an oily product, which could not be brought back to the crystalline state.

1-Isopropyl-2,5-dimethyl-4-cyano-4-piperidinol (XVI). A solution of 14.7 g sodium cyanide in 25 ml water was added to a solution of 20 g 1-isopropyl-2,5-dimethyl-4-piperidone (V) (b.p. 85-87° at 7 mm, n_D^{20} 1.4632) [3] in 75 ml 15% hydrochloric acid. When the sodium cyanide had been added, stirring was continued for a further hour at room temperature, after which the fine white crystalline precipitate was filtered off and washed twice with water. 10.9 g of cyanhydrin (XVI) was obtained. M.p. 106-108° (with liberation of gas) after recrystallization from ethyl acetate or benzine and drying in a vacuum desiccator.

Found %: N 14.50, 14.30. $C_{11}H_{20}ON_2$. Calculated %: N 14.28.

After the usual treatment the filtrate yielded a further 8.1 g of the cyanhydrin, identical with the main product, with m.p. 105-107°.

In all, this experiment yielded 19.0 g of cyanhydrin (XVI).

1-Allyl-2,5-dimethyl-4-cyano-4-piperidinol (XVII). A solution of 14.7 g sodium cyanide in 25 ml water was added to a solution of 30 g freshly distilled 1-allyl-2,5-dimethyl-4-piperidone (VI) (b.p. 87.5-88° at 7.5 mm, n_D^{20} 1.4740) [3] in 75 ml 15% hydrochloric acid. Stirring was continued for 1 hour at room temperature, the oily product extracted withe ether, the aqueous layer saturated with potassium carbonate and also extracted with ether. The combined ether extracts were dried, the ether distilled off, and a viscous oily amber colored residue obtained, which began to crystallize slowly when kept in a desiccator, forming gleaming rhombic crystals. Crystallization was accelerated by cooling with ice and rubbing the walls of the crystallization vessel with a glass rod.

34.2 g of the cyanhydrin (XVII) was obtained, which on recrystallization from benzine (b.p. 80-100°) separated slowly in the form of large crystals which liquefied to a transparent oil in the vacuum desiccator and then gradually solidified again to a snow-white crystalline mass. After 2 recrystallizations 22.0 g of cyanhydrin (XVII), m.p. 74-76°, was separated.

Found %: N 14.58, 14.73. $C_{11}H_{18}ON_2$. Calculated %: N 14.45.

Methiodide – fine snow-white clusters (from anhydrous alcohol), melting at 164-165° (decomp.).

Found %: N 8.53, 8.54. $C_{12}H_{21}ON_2I$. Calculated %: N 8.33.

On prolonged storage the mother liquors very slowly yielded a crystalline product, but an attempt to concentrate the solution resulted in the formation of an oily material which could not be crystallized.

1-Butyl-2,5-dimethyl-4-cyano-4-piperidinol (XVIII). A solution of 14.7 g sodium cyanide in 25 ml water was added to a solution of 20 g 1-butyl-2,5-dimethyl-4-piperidone (VII) (b.p. 80-81° at 3 mm, n_D^{20} 1.4630) [3] in 70 ml 15% hydrochloric acid. The oily product was extracted with ether, the aqueous layer saturated with potassium carbonate and also extracted with ether and the combined extracts dried with ignited sodium sulfate. After distillation of the ether the oily opalescent residue was stored in a desiccator and slowly crystallized. This yielded 21.2 g of cyanhydrin (XVIII) which on recrystallization from benzine (b.p. 80-100°) or ethyl acetate separated as very large glistening prismatic crystals melted at 69-71° and rapidly liquefying in the desiccator to form a transparent oil. On further storage the product solidified and formed a snow-white scaly mass. After 2 recrystallizations from benzine (b.p. 80-100°) 16.2 g of cyanhydrin (XVIII) with m.p. 82-83° was obtained.

Found %: N 13.52, 13.48. $C_{12}H_{22}ON_2$. Calculated %: N 13.33.

The mother liquor yielded more crystalline product which was further purified with great difficulty.

1-Isobutyl-2,5-dimethyl-4-cyano-4-piperidinol (XIX). A solution of 14.7 g sodium cyanide in 25 ml water was added to a solution of 20 g 1-isobutyl-2,5-dimethyl-4-piperidone (VIII) (b.p. 80-81° at 3.5 mm, n_D^{20} 1.4605) [3] in 70 ml 15% hydrochloric acid. Extraction of the oily reaction product with ether and the usual treatment yielded 22.1 g of the oily cyanhydrin (XIX) which was converted quantitatively into the original piperidone (VIII) when an attempt was made to purify it by vacuum distillation (at 2 and 10 mm). Repeated syntheses also led to the formation of an oily product which could not be crystallized. The cyanhydrin (XIX) was used in further reactions without preliminary purification.

1-Isoamyl-2,5-dimethyl-4-cyano-4-piperidinol (XX). A solution of 14.7 g sodium cyanide in 25 ml water was added to a solution of 19.7 g 1-isoamyl-2,5-dimethyl-4-piperidone (IX) (b.p. 90-92° at 2 mm, n_D^{20} 1.4615) [3] in 70 ml 15% hydrochloric acid. Extraction of the oily reaction product with ether and the usual treatment yielded an oily residue which crystallized when the crystallization vessel was cooled and the walls scraped with a glass rod. 22.3 g of cyanhydrin (XX) was obtained, which after 2 recrystallizations from petroleum ether separated as glistening plates which lost their luster and transparency when dried in a vacuum desiccator and melted at 85-87° (with evolution of gas).

Found %: N 12.71, 12.40. $C_{13}H_{24}ON_2$. Calculated %: N 12.50.

Methiodide melted at 166-167° (decomp.) after 2 recrystallizations from a mixture of anhydrous alcohol and acetone.

Found %: N 7.50, 7.72. $C_{14}H_{27}ON_2I$. Calculated %: N 7.65.

1-Cyclohexyl-2,5-dimethyl-4-cyano-4-piperidinol (XXI). A solution of 29.4 g sodium cyanide in 50 ml water was added to a solution of 64 g 1-cyclohexyl-2,5-dimethyl-4-piperidone (X) (m.p. 73-74.5°) [3] in 150 ml 15% hydrochloric acid. Towards the end of the sodium cyanide addition the whole mass thickened and rapidly solidified. The solid product was broken up, filtered off, washed with three portions of ice water and dried in a vacuum desiccator. This yielded 65 g cyanhydrin (XXI) which on recrystallization from ethyl acetate separated as gleaming plates melting at 108-109°.

Found %: N 11.81, 11.96. $C_{14}H_{24}ON_2$. Calculated %: N 11.86.

A further 1.5 g of less pure cyanhydrin (XXI) (m.p. 107-109°) was obtained from the aqueous filtrate by the usual treatment.

Methiodide after recrystallization from anhydrous alcohol melted at 184° (decomp.).

Found %: N 7.23, 7.27. $C_{15}H_{27}ON_2I$. Calculated %: N 7.47.

1-Phenyl-2,5-dimethyl-4-cyano-4-piperidinol (XXII). A solution of 29.4 g sodium cyanide was added to a solution of 68 g 1-phenyl-2,5-dimethyl-4-piperidone (XI) (b.p. 127-128° at 3.5 mm, n_D^{20} 1.5520) [3] in 150 ml 15% hydrochloric acid. After extraction of the oily reaction product with ether and the usual treatment 75.7 g of cyanhydrin (XXII) was obtained, which after 3 recrystallizations from ethyl acetate separated as solid glistening prisms, and separated from benzine (b.p. 80-100°) in the form of light glistening plates with m.p. 143-144°.

Found %: N 12.45, 12.60. $C_{14}H_{18}ON_2$. Calculated %: N 12.17.

1,2-Dimethyl-4-hydroxy-4-cyanodecahydroquinoline (XXV). A solution of 29.4 g of sodium cyanide in 50 ml water was added in the usual way to a solution of 62.2 g 1,2-dimethyl-4-ketodecahydroquinoline (XXIII) (b.p. 88-90° at 2.5 mm, n_D^{20} 1.4943 [1] in 150 ml 15% hydrochloric acid. When the sodium cyanide had been added, stirring was continued for 2 hours at room temperature. The viscous oily reaction product thickened as stirring continued and finally solidified completely. The crystalline mass was broken up, filtered off, washed twice with ice water and dried in a vacuum desiccator. 62.2 g of cyanhydrin (XXV) was obtained, which after recrystallization from ethyl acetate separated as snow-white needles with m.p. 119-120°.

Found %: N 13.73, 13.60. $C_{12}H_{20}ON_2$. Calculated %: N 13.46.

The usual treatment of the aqueous filtrate yielded a further 7.1 g of oily cyanhydrin (XXV) in the form of a viscous material with a characteristic amine odor. In all, this experiment yielded 69.3 g of cyanhydrin (XXV).

Methiodide – after 2 recrystallizations from absolute alcohol – needle-shaped crystals with m.p. 176-177°.

Found %: N 8.36, 7.74. $C_{13}H_{23}ON_2I$. Calculated %: N 8.00.

1,2-Dimethyl-4-hydroxy-4-cyanoperhydropyrindine (XXVI). A solution of 14.7 g sodium cyanide in 25 ml water was added in the usual way to a solution of 26 g 1,2 -dimethyl-4-ketoperhydropyrindine (XXIV) (b.p. 85-86° at 2 mm. n_D^{20} 1.4912[2] in 75 ml 15% hydrochloric acid. When the sodium cyanide had been added stirring was continued at room temperature for 2 hours. The oily product was extracted with ether and after the usual treatment 29 g of the cyanhydrin (XXVI) was obtained, which after recrystallization from ethyl acetate separated as glistening crystalline needles with m.p. 135-136°.

Found %: N 14.67, 14.73. $C_{11}H_{19}ON_2$. Calculated %: N 14.43.

2,2-Dimethyl-4-cyanotetrahydropyran-4-ol (XXXI). A solution of 29.4 g sodium cyanide in 50 ml water was added dropwise with cooling by ice and constant stirring over a period of 1 hour to a mixture of 61 g 2,2-dimethyltetrahydropyran-4-one (XXVII) (b.p. 178-179° at 760 mm, n_D^{20} 1.4470)[4] and 155 ml 40% sodium bisulfite solution. After the addition of the sodium cyanide, stirring was continued for a further hour at room temperature. The oily product was extracted with ether, the aqueous layer saturated with sodium chloride and also extracted with ether. The combined ether extracts were then shaken up with 50 ml saturated aqueous bisulfite solution and then with concentrated sodium chloride solution. The ether extract was dried and the ether distilled off, giving 50.5 g of transparent pale yellow oily cyanhydrin (XXXI), which soon crystallized completely to a solid mass with a characteristic odor. After recrystallization from benzene the product separated as large prismatic crystals with m.p. 84-85°.

Found %: N 8.83, 8.84. $C_9H_{15}O_2N$. Calculated %: N 9.03.

2,2-Dimethyl-4-cyanotetrahydrothiopyran-4-ol (XXXII). 155 ml 40% sodium bisulfite was added to 57.6 g 2,2-dimethyltetrahydrothiopyran-4-one (XXVII) (b.p. 66-67° at 3.5 mm, n_D^{20} 1.4910) [5]. When one third of bisulfite had been added, the formation of long silky needles of the crystalline bisulfite compound (XXX) began and was complete after 2 hours, while the reaction mass simultaneously became extremely thick. A solution of 29.4 g of sodium cyanide in 50 ml water was then added dropwise with cooling by ice and uninterrupted stirring to the bisulfite compound, and stirring continued for 2 hours at room temperature. The oily product was extracted with ether. The combined ether extracts were washed with 100 ml saturated sodium bisulfite solution and then with a saturated sodium chloride solution and dried with ignited sodium sulfate. The oily residue from the distillation of the ether rapidly crystallized. 48.5 g of cyanhydrin (XXXII) was obtained, which after recrystallization from benzine (b.p. 80-100°) separated as star-shaped clusters of needles with m.p. 76-76.5°.

Found %: N 8.21, 8.42. $C_9H_{15}ONS$. Calculated %: N 8.19.

SUMMARY

The reaction of γ-piperidones, tetrahydro-γ-pyrones and tetrahydro-γ-thiopyrones with hydrogen chloride leads easily to the formation in good yield of the corresponding cyanhydrins, which are of considerable interest as intermediate products in the synthesis of new anesthetic substances with the α-eucaine structure.

It has been shown that the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones has a spatially directed character and leads to the formation, in yields of up to 97%, of one of four theoretically possible stereoisomeric forms of the corresponding cyanhydrins.

The strict stereochemical directivity of the addition of hydrogen cyanide to 1-alkyl-2,5-dimethyl-4-piperidones is explained by the fact that these γ-piperidones, under the conditions of the cyanhydrin synthesis (acid or neutral medium), react in only one stereoisomeric form, and the addition of hydrogen cyanide to the carbonyl group of 1-alkyl-2,5-dimethyl-4-piperidones takes place predominantly in one direction—from the side which is less screened, opposite to the neighboring methyl group.

The formation of isomers in other addition reactions at the carbonyl group in 1-alkyl-2,5-dimethyl-4-piperidones which take place in alkaline medium, is explained by the reversible isomerization of these piperidones involving their enolization and the related inversion of spatial configuration.

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STUDIES IN THE FIELD OF HETEROCYCLIC CHEMISTRY

XXVI. NEW METHODS FOR PREPARING 9-PHENYLACRIDINE

P. A. Petyunin and N. G. Panferova

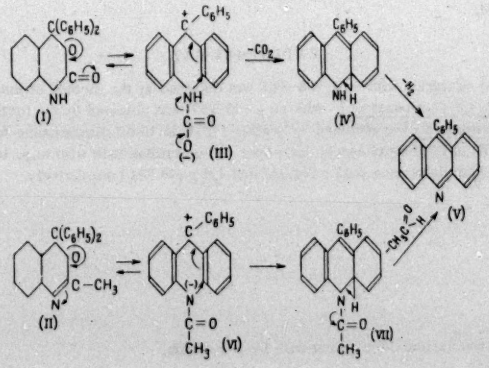
Methods for preparing 9-phenylacridine based on 2-aminotriphenylcarbinol and its acyl derivatives have recently been worked out by M. E. Konshin and ourselves [1,2]. In the present work diphenylisatoic acid anhydride (I) and 2-methyl-6,6-diphenyl-[benzo- 1',2': 4,5-(1,3-oxazine)] (II) have been used as starting materials for the preparation of 9-phenylacridine.

(I) and (II) contain a similar system of conjugated bonds ($\geq C-\overset{\frown}{O}-\underset{|}{C}=\overset{\frown}{y}$, where y = oxygen or nitrogen)

which makes up part of the heterocyclic chain. It is true that in compound (I) the oxygen with the double bond is situated outside the ring. Both these compounds are derivatives of 4,5-benzomethoxazine. The structural similarity of (I) and (II), and their property of undergoing acidolysis with the formation of 2-amino-triphenylcarbinol [3,4] indicates the possibility of using them for the synthesis of 9-phenylacridine. To achieve this it has been necessary to find conditions under which the opening of the heterocyclic ring (dissociation at the

$\geq C \rightarrow O -$ bond) would take place without blocking the nucleophilic reaction center ($>$NH group). In this case acids proved to be unsuitable, since in opening the heterocyclic ring they link up with the amino group and remove it from the sphere of reaction.

The problem was solved by carrying out the experiments in nitrobenzene. In this way 9-phenylacridine was obtained in 65-70% yield. The reaction mechanism may be represented in the following way:



In accordance with the scheme shown, (I) and (II) are converted into 9-phenylacridine (V) by an ionic mechanism. Compounds (I) and (II), like triarylcarbinols, contain the "loose" bond Ar_3C-O; it may therefore, be assumed that in polar aprotic solvents (for example nitrobenzene) they will dissociate at this bond in the same way as triarylcarbinols and their condensation products [5]. The acridine ring closes in the ionic complexes (III) and (VI). Hydrogen or acetaldehyde splits off from the intermediate products (IV) and (VII) forming (V).

It should be noted that the synthesis of 9-phenylacridine from (I) and (II) is not described in the literature. From the theoretical aspect it has been interesting to make a comparison of the ease of closure of the acridine ring in 2-aminotriphenylcarbinol (VIII), its N-acetyl derivative (IX) and 2-methyl-6,6-diphenyl-[benzo-1',2': 4,5-(1,3-oxazine)] (II).* The data thus obtained are given in the Table.**

Starting material	Yield of 9-phenylacridine (%)			
	Time of heating (in minutes)			
	5	10	30	60
(VIII)	87.3	90.6	94.9	97.08
(IX)	Traces	Traces	77.1	77.1
(II)	—	Traces	64.5	70.4

From the data in the Table it can be seen that the ease of closure of the acridine ring decreases in the order: (VII)> (IX)> (II). Compound (IX) contains a weaker nucleophilic reactive center ($-NHCOCH_3$) than (VIII) and, as would be expected, the acridine ring closes less readily in this case. Thus, when the reaction mass is heated for 5 minutes, 9-phenylacridine is obtained in 87.3% yield from (VIII), while only traces are obtained from (IX). The reduction in the rate of conversion of (II) is probably explained by the more difficult dissociation. The formation of (V) is observed after heating the original materials for 30 minutes, and the reaction product is obtained in lower yield.

EXPERIMENTAL

Diphenylisatoacid anhydride with m.p. 238-239° was obtained by the method of Inagaki [3]. 2-Methyl-6,6-diphenyl-[benzo-1,2:4,5-(1,3-oxazine)] with m.p 135-137° was obtained by the method of Baeyer and Villiger [4]. 9-Phenylacridine (V) was obtained by heating 1 g (I) in 10 ml nitrobenzene for 2 hours on a sand bath, or by heating 3 g (II) in 3 ml nitrobenzene for 1 hour. The acridine base with m.p. 182-185.5° was isolated as in previous work [1]. The yields were 0.55 g (64.9%) and 1.8 g (70.35%) respectively.

* This part of the work was carried out together with M. E. Konshin.

** The experiments were carried out under identical conditions: in each experiment 1 g of material and 1 ml nitrobenzene were taken.

SUMMARY

1. New methods for preparing 9-phenylacridine from diphenylisatoacid anhydride and 2-methyl-6,6-di-phenyl [benzo-1',2' : 4,5-(1,3-oxazine)] have been worked out.

2. A reaction mechanism has been suggested and discussed.

3. The comparative ease of closure of the acridine ring in (VIII), (IX) and (II) has been studied; it has been established that the rate of closure of the acridine ring decreases in the order : (VIII)> (IX)> (II).

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

VII. SILICOANHYDRIDES OF UNSATURATED MONOBASIC ORGANIC ACIDS IN THE SYNTHESIS OF UNSATURATED KETONES OF THE BENZENE, THIOPHEN AND SELENOPHEN SERIES

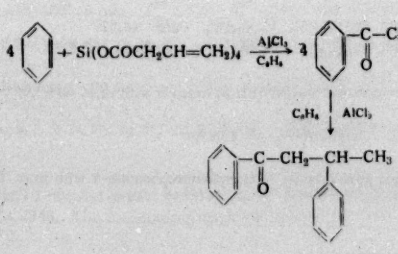
Yu. K. Yuryev, G. B. Elyakov and I. M. Milshtein

The unsaturated ketones of the thiophen series have been little studied. In 1947 Hartough et al. [1] obtained propenyl 2-thienyl ketone in 22% yield by the acylation of thiophen with crotonyl chloride in the presence of montmorillonite clay. Later, Bradscher, Brown and Grantham [2] obtained this ketone in 64% yield by the acylation of thiophen with crotonyl chloride in the presence of stannic chloride. Hartough and Kosak [3] in 1937 described the direct acylation of thiophen with an unsaturated acid: $\Delta^{9,10}$-octadecenyl 2-thienyl ketone was prepared in 55% yield by the reaction of $\Delta^{9,10}$-octadecenic acid and thiophen in the presence of phosphorus pentoxide.

Only one representative of the unsaturated ketones of the selenophen series is known – styrl 2-selenienyl ketone, obtained by Umesawa [4] by the condensation of benzaldehyde with methyl 2-selenienyl ketone in hydrochloric acid. The yield of this ketone is not given by the author.

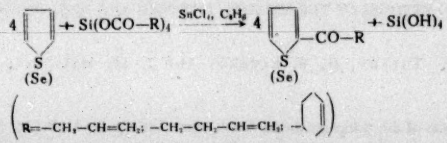
In previous works we have shown the possibility of conveniently acylating thiophen [5] and selenophen [6] with the mixed anhydrides of orthosilicic and monobasic saturated organic acids. The similar reaction with the silicoanhydrides of unsaturated acids has not been studied and interest has therefore been attached to preparing these materials and using them for the acylation of benzene, thiophen and selenophen.

In the acylation of benzene with vinylacetyl silicoanhydride in the presence of anhydrous aluminum chloride, one might expect the formation of α-tetralone, which could be formed as the result of intramolecular alkylation of the allyl phenyl ketone formed, with closure of the tetralone ring. We have established, however, that this reaction does not take place if the acylation is carried out in an excess of benzene as solvent. When benzene is acylated with vinylacetyl silicoanhydride in this way, two reaction products are obtained: the unsaturated ketone – allyl phenyl ketone, which is not described in the literature, and the saturated aliphatic - aromatic ketone – 3-phenylbutyrophenone-1, which is formed by alkylation of the benzene present in excess of the unsaturated ketone:



When thiophen and selenophen are acylated with the silicoanhydrides of unsaturated acids in benzene in the presence of anhydrous stannic chloride, the possibility of a similar alkylation of the thiophen or selenophen nucleus is largely excluded as a result of the comparatively low ability of stannic chloride to catalyze the alkylation by olefines of the thiophen or selenophen nucleus, or its even lower ability to catalyze the alkylation of benzene.

It has been shown in the present work that the acylation of thiophen and selenophen with the silicoanhydrides of vinylacetic, γ, δ-pentenylic and Δ^3-cyclohexenecarboxylic acids leads to the formation of only the corresponding unsaturated ketone in 20-30% yield, so that the presence of a double bond in the β, γ-or γ, δ-position has little effect on the yield of ketone.



Using the method evolved in the present work we have prepared the following unsaturated ketones of the thiophen and selenophen series, which are not described in the literature: allyl 2-thienyl ketone (20%), α-butenyl 2-thienyl ketone (30%), and Δ^3-cyclohexenyl 2-thienyl ketone (33%); allyl 2-selenienyl ketone (30%), α-butenyl 2-selenienyl ketone (23%) and Δ^3-cyclohexenyl 2-selenienyl ketone (30%).

The unsaturated ketones of the thiophen and selenophen series are liquids of a pale yellow color, rapidly darkening in air.

EXPERIMENTAL

The acylation of benzene with vinylacetyl silicoanhydride 150 ml dry benzene. 8.6 g (0.1 mole) vinylacetic acid and 4.3 g (0.025 mole) silicon tetrachloride were placed in a three-necked flask (250 ml) fitted with a stirrer and reflux condenser with calcium chloride tube. This was heated on a water bath until the evolution of hydrogen chloride had ceased, cooled with ice water, and 27 g finely divided aluminum chloride added over a period of 30 minutes. The reaction mass was heated on the water bath until evolution of hydrogen chloride had ceased, cooled and decompcsed by pouring on to 200 g ice with 20 ml concentrated hydrochloric acid. The benzene layer was decanted, the residue filtered through cotton waste and the precipitate extracted with benzene for 6 hours in an extractor. The filtrate was saturated with sodium chloride and extracted with benzene. The combined benzene extracts were washed with 15% caustic soda solution and water and dried with calcium chloride. The benzene was distilled off and the residue vacuum distilled to give the following fractions: 1st, b.p. 115-135° (10 mm), 2.9 g; 2nd, b.p. 135-160° (10 mm), 1 g; 3rd, b.p. 160-165° (10 mm), 3.15 g.

When the 1st and 2nd fractions were vacuum distilled again, 2.4 g (17%) of allyl phenyl ketone was obtained:

B.p. 104° (5 mm), n_D^{20} 1.5577, d_4^{20} 1.0630, MR_D 44.33. $C_{10}H_{10}O$. calc. 44.32.
Found %: C 82.07, 81.87; H 7.09, 7.08. $C_{10}H_{10}O$. Calculated %: C 82.13; H 6.93.

Allyl phenyl ketone 2,4-dinitrophenylhydrazone—bright yellow crystals with m.p. 204-205°.

Found %: N 17.25, 17.31. $C_{16}H_{14}O_4N_4$. Calculated %: N 17.17.

The 3rd fraction crystallized rapidly and proved to be 3-phenylbutyrophenone-1 with m.p. 72.5° (from methanol). Yield 14% of theoretical.

Found %: C 85.77, 85.80; H 7.25, 7.28. $C_{16}H_{16}O$. Calculated %: C 85.67; H 7.19.

Litorature data for 3-phenylbutyrophenone-1: m.p. 70° [7]; 71-72° [8].

The acylation of thiophen. Working method. 70 ml dry benzene, 0.06 mole unsaturated acid and 0.015 mole silicon tetrachloride were placed in a three-necked flask (100 ml) fitted with a stirrer, reflux condenser with calcium chloride tube, and dropping funnel, and heated on a water bath until evolution of hydrogen chloride had ceased. The mixture was cooled with ice water and 0.05 mole thiophen added, followed by 0.025 mole anhydrous stannic chloride in 15 ml dry benzene, added dropwise. The mixture was then either stirred at room temperature or heated on the water bath (see below)—depending on the ketone obtained—then decomposed by pouring on to 100 g ice and steam distilled. The distillate was saturated with sodium chloride and extracted with ether; the ether extract and the benzene distillate were washed with 15% caustic soda solution and water and dried with calcium chloride. The benzene was then distilled off, the ether extract added to the residue, the solvent distilled off and the residue vacuum distilled.

Allyl 2-thienyl ketone. 1.6 g (20%) allyl 2-thienyl ketone was obtained from 5.16 g vinylacetic acid, 2.55 g silicon tetrachloride, 4.2 g thiophen and 6.5 g stannic chloride by heating the reaction mass (after addition of the stannic chloride) for 1 hour at room temperature:

b. p. 104.5-105° (3 mm), n_D^{20} 1.5945, d_4^{20} 1.1420.* MR_D 45.27. C_8H_8OS. calc. 43.52. Found %: S 21.06. C_8H_8OS. Calculated %: S 21.06.

2,4-dinitrophenylhydrazone—red crystals: m.p. 170-171°.*

Found %: N 16.79, 16.86. $C_{14}H_{12}O_4SN_4$. Calculated %: N 16.86.

α-Butenyl 2-thienyl ketone. 2.5 g (30%) α-butenyl 2-thienyl ketone was obtained from 6 g γ,δ-pentenylic acid, 2.55 g silicon tetrachloride, 4.2 g thiophen and 6.5 g stannic chloride by stirring the reaction mass (after introduction of all the stannic chloride) for half an hour at room temperature, and afterwards for 45 minutes on the water bath at 80° (thermometer in bath):

b. p. 123-124° (10 mm); n_D^{20} 1.5585; d_4^{20} 1.1130. MR_D 48.19. $C_9H_{10}OS$. calc. 48.14.

Found %: S 18.85. $C_9H_{10}OS$. Calculated %: S 19.19.

2,4-Dinitrophenylhydrazone—red needles: m.p. 136-137°.

Found %: N 16.24, 16.38. $C_{15}H_{14}O_4SN_4$. Calculated %: N 16.17.

Δ^3-Cyclohexenyl 2-thienyl ketone. 3.2 g (33%) Δ^3-cyclohexenyl 2-thienyl ketone was obtained from 7.56 g Δ^3-cyclohexenecarboxylic acid, 2.55 g silicon tetrachloride, 4.2 g thiophen and 6.5 g stannic chloride by stirring (after addition of all the stannic chloride) for half an hour at room temperature and then heating for 2 hours on a boiling water bath:

b. p. 155-156° (8 mm); n_D^{20} 1.5790, d_4^{20} 1.1600, MR_D 55.00. $C_{11}H_{12}OS$. Calc. 55.18.

Found %: S 16.82. $C_{11}H_{12}OS$. Calculated %: S 16.67.

2,4-dinitrophenylhydrazone—yellow needles: m. p. 176°.

Found %: N 14.70, 14.61. $C_{17}H_{16}O_4SN_4$. Calculated %: N 15.04.

* The propenyl 2-thienyl ketone described in the literature had the following constants: b.p. 134.5-135.5° (14 mm), n_D^{25} 1.5949. The 2,4-dinitrophenylhydrazone of this ketone melted at 183-184° [1].

The Acylation of Selenophen. The working method differed from that described above for thiophen in that the stannic chloride was first added to the silicide solution followed by dropwise addition of the solution of selenophen in benzene, with cooling by ice water.

Allyl 2-selenienyl ketone. 1.6 g (30%) allyl 2-selenienyl ketone was obtained from 5.16 g vinylacetic acid, 2.55 g silicon tetrachloride, 3.9 g stannic chloride and 4 g selenophen by decomposing the reaction mass with ice as soon as its temperature (on removal of the coolant) reached room temperature.

b.p. 128° (11 mm), n_D^{20} 1.5990, d_4^{20} 1.4220, MR_D 47.77. $C_8H_8OSeF_3$. Calc. 46.16.

Found %: C 48.62, 48.76; H 4.44, 4.50. C_8H_8OSe. Calculated %: C 48.26; H 4.10.

2,4-Dinitrophenylhydrazone – deep red needles: m.p. 174-175°.

Found %: N 14.58, 14.42. $C_{14}H_{12}O_4SeN_4$. Calculated %: N 14.77.

α-Butenyl 2-selenienyl ketone. 2 g (23%) α-butenyl 2-selenienyl ketone was obtained from 5 g γ,δ-pentenylic acid, 2.55 g silicon tetrachloride, 3.9 g stannic chloride and 4 g selenophen by stirring for 15 minutes at room temperature (after addition of the selenophen), warming for 45 minutes on a water bath at 60° (thermometer in bath) and then pouring the mixture into ice.

b.p. 116-117° (5 mm), n_D^{20} 1.5760, d_4^{20} 1.3640, MR_D 51.69. $C_9H_{10}OSeF_3$. Calc. 50.78.

Found %: C 51.38, 51.44; H 5.00, 5.26. $C_9H_{10}OSe$. Calculated %: C 50.72; H 4.73.

2,4-Dinitrophenylhydrazone – deep red needles: m.p. 155°.

Found % N 13.91, 13.89. $C_{15}H_{14}O_4SeN_4$. Calculated %: N 13.93.

Δ^3-Cyclohexenyl 2-selenienyl ketone. 2.1 g (30%) Δ^3-cyclohexenyl 2-selenienyl ketone was obtained from 5.8 g Δ^3-cyclohexenecarboxylic acid, 2.55 g silicon tetrachloride, 3.9 g stannic chloride and 4 g selenophen by decomposing the reaction mass with ice as soon as it reached room temperature (after removal of the coolant).

b.p. 151-152° (6 mm), n_D^{20} 1.5800, d_4^{20} 1.3650, MR_D 58.18. $C_{11}H_{12}OSeF_3$. Calc. 57.81.

Found %: C 55.48, 55.61; H 5.17, 5.10. $C_{11}H_{12}OSe$. Calculated %: C 55.22; H 5.06.

2,4-Dinitrophenylhydrazone – yellow needles: m.p. 177-177.5°.

Found %: N 13.76, 13.78. $C_{17}H_{16}O_4SeN_4$. Calculated %: N 13.36.

SUMMARY

1. Unsaturated monobasic organic acids react with silicon tetrachloride in the same way as the saturated acids, forming the corresponding silicoanhydrides.

2. Unsaturated ketones of the benzene, thiophen and selenophen series can be prepared by the acylation of benzene, thiophen and selenophen respectively with the silicoanhydrides of unsaturated monobasic organic acids.

3. The following have been prepared for the first time, using the silicoanhydrides of unsaturated monobasic organic acids: allyl phenyl ketone, allyl 2-thienyl ketone, α-butenyl 2-thienyl ketone, Δ^3-cyclohexenyl 2-thienyl ketone, allyl 2-selenienyl ketone, α-butenyl 2-selenienyl ketone, and Δ^3-cyclohexenyl 2-selenienyl ketone.

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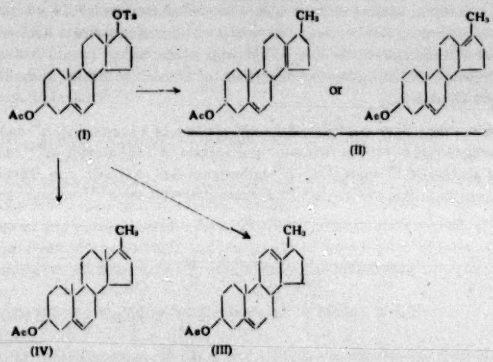
SOME PROPERTIES OF p-TOLUENESULFONATES OF 17β-HYDROXYSTEROIDS

VI. THE SYNTHESIS OF THE ACETATE OF 17,17-DIMETHYL-18-NOR-$\Delta^{5,12}$-ANDROSTADIENOL-3

O. S. Madaeva

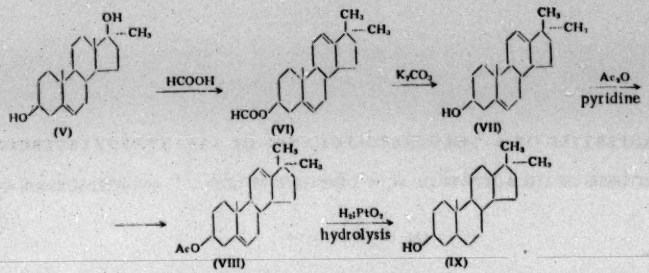
In connection with work devoted to an examination of the direction of reaction in the separation of p-toluenesulfonic acid from the 3-acetate 17-tosylate of Δ^5-androstenediol-3β, 17β (I) [1], it became necessary to prepare the isomeric compounds whose formation is possible in this reaction:



One of these is the acetate of 17-methyl-18-norandrostadienol-3 (III) whose synthesis is difficult to carry out. Inasmuch as we have shown [2] that the introduction of a double bond in the 12–13 position of 17α-methylandrostanediol-3β,17 is extremely easily achieved, work was carried out on the synthesis of the acetate of 17,17-dimethyl-$\Delta^{5,12}$-androstadienol-3β (VIII)—the homolog of isomer (III)—which we assumed could serve as a structural model for spectroscopic studies on the products obtained from the removal of p-toluenesulfonic acid from (I).

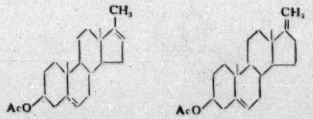
The starting material was 17α-methyl-Δ^5-androstenediol-3β,17 (V), and on heating this with anhydrous formic acid dehydration took place at the C_{17} atom with the formation of the formate of 17,17-dimethyl-$\Delta^{5,12}$-androstadienol-3β (VI). Hydrolysis of the latter with a solution of potassium carbonate in aqueous methanol led to the formation of 17,17-dimethylandrostadienol-3β (VII). The acetate of this (VIII) was obtained by the reaction of (VII) with acetic anhydride in pyridine solution.

The elementary composition of this substance corresponds to the acetate of the product of the dehydration of (V).



To establish the structure of (VIII), its double bonds were exhaustively hydrogenated with hydrogen in glacial acetic acid in the presence of previously reduced platinum oxide. The substance (IX) isolated after this reaction was identical in crystalline form, melting point and specific rotation with 17,17-dimethyl-18-norandrostanol-3β, which we obtained on hydrolysing the product of dehydration of 17α-methylandrostandiol-3β,-17 by heating the latter with formic acid [2]. A mixture of (IX) with 17,17-dimethyl-18-norandrostanol-3β gave no melting point depression, while a mixture with 17α-methylandrostanol-3β melted below its melting point. In this way it was confirmed that heating 17α-methyl-Δ^5-androstenediol-3β,17 with formic acid also brings about a retropinacol rearrangement leading to a change in the carbon steroid skeleton. The absence of a blue coloration with nitrosyl chloride under the conditions of Thiele's reaction [3] shows that the double bond formed in this way is not ditertiary.

Thus, at the present time three products of the dehydration of 17α-methyl-Δ^5-androstenediol-3β,17 are known: two with unchanged carbon steroid structure – the acetate of 17α-methyl-$\Delta^{5,16}$-androstadienol-3 (X) with m.p. 134-135°, and the acetate of 17-methylene-Δ^5-androstenol-3 β (XI) with m.p. 95-96° [4], and the product of retropinacol rearrangement referred to above – 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3 (VIII).



A substance with m.p. 55-56°, $[\alpha]_D^{22}$ – 185° (1.7%, in chloroform), corresponding in elementary composition to the product of dehydration of 17α-methyl-Δ^5-androstendiol-3β,17, has been described in the literature [4]. This was obtained together with (X) and (XI) by chromatographing the reaction product after boiling (V) with acetic anhydride in the presence of pyridine, and its hydrogenation product gave a melting point depression with 17α-methylandrostanol-3β. On this basis the authors suggest that the dehydration of (V) took place accompanied by a retropinacol rearrangement and that the substance with m.p. 55-56° is an isomer of (X) or (XI) with a changed carbon steroid skeleton.

EXPERIMENTAL

Formate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (VI). 5 g 17α-methyl-Δ^5-androstenediol-3β,17 with m.p. 200-203° was heated with 15 ml 98% formic acid for 5 minutes at 100°. The residue at first turned pink, then became violet, while after two minutes a layer of oil rose to the surface and the lower formic acid layer turned green. The mixture was cooled, poured into water, extracted with ether, the ether extract washed with water, then with 2% sodium bicarbonate solution, again with water and dried with sodium sulfate. 4.65 g of a pale yellow oil was obtained, which crystallized immediately on the addition of methanol. The residue was recrystallized from 56 ml methanol, yielding 2.8 g with m.p. 105.5-106°, while a further 0.45 g with m.p. 102-105.3° was isolated from the filtrate. After a second recrystallization from methanol, needles with m.p. 107-107.5° were obtained.

Found %: C 79.90; H 9.55. $C_{21}H_{30}O_2$. Calculated %: C 80.18; H 9.54.

The residue of 1.2 g from the filtrates was dissolved in 12 ml of a mixture of benzine (b.p. 80-100°) and benzene (1:1) and passed through a column with 15 g alumina. The same solvents were used as eluent. The oil obtained crystallized after distillation of the solvent. Recrystallization from ethyl acetate yielded 0.7 g material with m.p. 129.5-130.5° (plates). A mixture with the hydrolyzed formate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (VII) gave no melting point depression.

17,17-Dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (VII). 2.8 g (VI) with m.p. 105.5-106.5° was boiled for 1 hour 15 minutes with 24.4 ml methanol and an aqueous potassium carbonate solution (1.76 g in 7 ml water). The precipitate which separated from the reaction solution on cooling was filtered off, washed with water and dried in vacuo at 60°. 2.17 g with m.p. 131.5-132.5° was obtained, while the filtrate yielded a further 0.3 g with m.p. 129-130° when diluted with water. The combined precipitates were recrystallized from ethyl acetate: fine plates, m.p. 133-133.5°.

Found %: C 83.76; H 10.47. $C_{20}H_{30}O$. Calculated %: C 83.85; H 10.55.

Acetate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (VIII). 1 g (VII) was dissolved in 4 ml dry pyridine, 1 ml acetic anhydride added and the solution obtained left for 24 hours at room temperature. It was then decomposed with water and extracted with ether. The ether extracts were washed, dried and the ether distilled off. 1.02 g of precipitate was obtained and recrystallized from 6 ml methanol. This yielded 0.92 g, with m.p. 78-78.5° (prisms from methanol), $[\alpha]_D^{20} -176.4°$ (2 %, in chloroform).

Found %: C 80.50, H 9.78. $C_{22}H_{32}O_2$. Calculated %: C 80.43; H 9.82.

17,17-Dimethyl-18-norandrostanol-3β (IX). 0.3 g (VIII) was dissolved in 6 ml glacial acetic acid and hydrogenated with previously reduced platinum oxide (0.05 g) in 10 ml acetic acid. A quantity of hydrogen corresponding to 1 mole was absorbed in 1 hour. After filtration of the catalyst and distillation of the acetic acid in vacuo, the colorless oil obtained was dissolved in ether, the ether solution washed with water, then with 2% sodium bicarbonate solution and again with water, dried with sodium sulfate and the ether distilled off. This yielded 0.32 g of oily uncrystallized residue which gave no yellow coloration with tetranitromethane.

For the hydrolysis of the acetyl group, 0.32 g of the substance obtained was dissolved in 15 ml methanol and boiled with a solution of 0.2 g ignited potassium carbonate in 3 ml water for 1 hour 15 minutes. Towards the end of the reaction a white precipitate was formed and filtered off after cooling. The precipitate which was obtained by diluting the filtrate with water was added to the main precipitate and 0.3 g material with m.p. 126-128° was obtained. M. p. 132-133° after two recrystallizations from acetone. The precipitate dissolved readily in alcohol and in methanol, less readily in benzine. Crystallized from ethyl alcohol as clusters of fine needles.

Found %: C 82.58; H 11.78. $C_{20}H_{34}O$. Calculated %: C 82.68; H 11.80.

SUMMARY

The acetate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β has been prepared by the hydrolysis of 17α-methyl-Δ^{5}-androstenediol.

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SOME PROPERTIES OF p-TOLUENESULFONATES OF 17 β-HYDROXYSTEROIDS

VII. INFRA-RED SPECTRA OF SOME DERIVATIVES OF THE ANDROSTANE AND 18-NORANDROSTANE SERIES

O. S. Madaeva and Yu. N. Sheinker

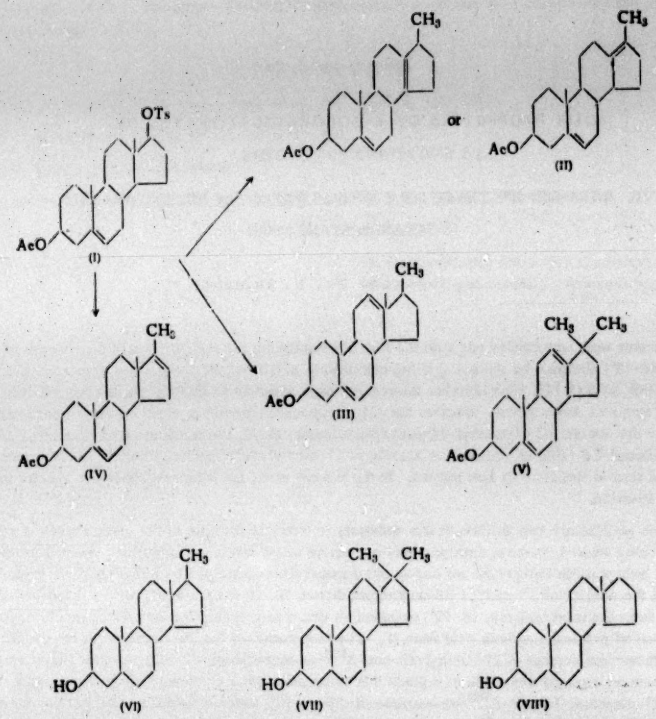
The present work was carried out with the aim of establishing the composition of the mixture of substances (m.p. 68-73°) obtained by removing p-toluenesulfonic acid from the 17-tosylate 3-acetate of Δ^{5}-androstenediol-3β, 17β (I) [1]. Considerable interest has been attached to finding how the process of p-toluenesulfonic acid removal takes place: whether the only compounds formed are those resulting from a retropinacol rearrangement – the acetate of 17-methyl-18-norandrostadienol-3β (II) and the acetate of 17-methyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (III), or whether the acetate of 17-methyl-$\Delta^{5,16}$-androstadienol-3β (IV) – a compound with unchanged steroid skeleton – is also formed. In the present work, the infra-red absorption spectra were used to resolve this question.

To reach satisfactory conclusions, it was necessary to have, in addition to the spectrum of the mixture (m.p. 68-73°) being studied, spectral data on every compound whose formation might be expected in this reaction. Of all such possible compounds we had at out disposal the acetate of 17-methyl-$\Delta^{5,16}$-androstadienol-3β (IV) [2] and the acetate of 17-methyl-18-norandrostadienol-3β (II) (m.p. 95-96°) with a ditertiary double bond, isolated from the mixture (m.p. 68-73°) obtained on chromatographing the acetylated reaction products from the removal of p-toluenesulfonic acid from (I). The preparation of the 3rd isomer with the double bond in the 12–13 position – the acetate of 17-methyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (III) proved difficult to achieve and for this reason an attempt was made to replace this compound with a compound of similar structure – the acetate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (V) [3], which differs from (III) only by the presence of an extra methyl group in position 17.

In order to confirm the validity of this replacement, a preliminary examination was made of the influence of the presence of a methyl group in the 17 position for androstanol-3β and its 17-methyl derivatives [2].

The infra-red spectra of 17-methylandrostanol-3β (VI) and 17,17-dimethyl-18-norandrostanol-3β (VII) were taken and a comparison made with the infra-red spectrum of androstanol-3β (VIII), which is given in the literature [4] (Fig. 1). A comparison of the spectra of these three compounds shows that the introduction of either one or two methyl groups into the 17 position of the androstane series brings about only a slight shift of the absorption bands without greatly altering the character of the spectra. Thus, it may be assumed that the acetate of 17,17-dimethyl-$\Delta^{5,12}$-androstadienol-3β can be used as a model compound instead of the acetate of 17-methyl-18-nor-$\Delta^{5,12}$-androstadienol-3β in a comparison of infra-red spectra.

A comparison of the infra-red spectra of the mixture (m.p. 68-73°) and of the compound with the ditertiary double bond (II) (Figure 2) showed that the mixture is composed chiefly of the latter. This follows from the complete coincidence of all the principal bands in the spectrum and the close resemblance in the whole character of the spectrum. However, some less intense bands which are present in the spectrum of the mixture are missing from that of the individual compound with the ditertiary double bond and evidently result



from the presence in the mixture of some other constituent, which may be compounds (III) and (IV), in addition to (II). Examples of such bands are those at 808, 843, 945, 960, 1081, 1136 and 1200 cm^{-1}.

To establish the nature of this other constituent, the spectrum of the mixture being studied was compared with the spectra of the compounds (IV)* and (V) referred to. From this comparison (Figure 2) it is seen that compound (IV) cannot be part of the mixture, since although it has many bands in its spectrum coinciding with bands in that of the mixture (bands which are general for all acetates of the androstadienol-3β series) it has in addition fairly pronounced bands, 802, 877, 913 and 1099 cm^{-1}, which are missing from the spectrum of the mixture.

* The infra-red spectrum (IV) obtained by us coincides fully with the infra-red spectrum given by Julia and Heusser [5].

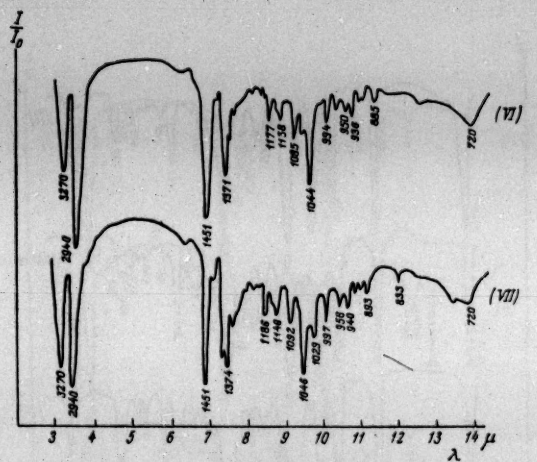
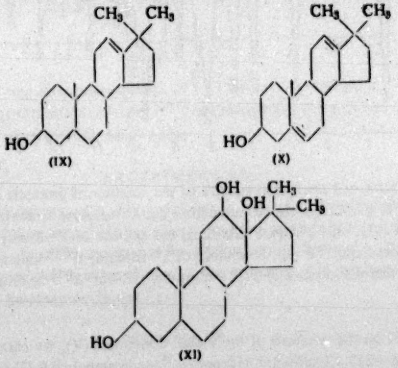


Fig. 1. Infra-red absorption spectra of 17-methylandrostanol-3 β (VI) and 17,17-dimethyl-18-norandrostanol-3β (VII).



On the other hand, the spectrum of compound (V) has, in addition to the bands which are common to all compounds of this series, all the bands which characterize the additional constituent of the mixture being studied (808, 847, 945, 960, 1086, 1138 and 1200 cm^{-1}). This gives grounds for supposing that the second product of retropinacol rearrangement—the acetate of 17-methyl-Δ^{5+11}-androstadienol-3β (III)—is present in the mixture as an additional constituent.

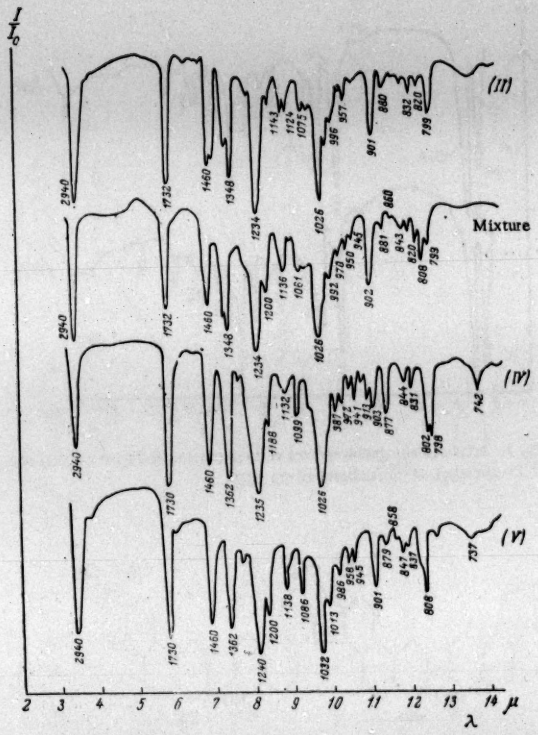


Fig. 2. Infra-red absorption spectra of the mixture of products obtained on removal of p-toluenesulfonic acid from the 17-tosylate 3-acetate of Δ^5-androstenediol-3β, 17β (the mixture), the acetate of 17-methyl-18-norandrostadienol-3β (II), 3-acetate of 17-methyl-$\Delta^{5,16}$-androstadienol-3β (IV) and the acetate of 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β (V).

In the course of work on the synthesis of the model compound (V), we obtained several other derivatives of the 18-norandrostane series – 17,17-dimethyl-18-nor-Δ^{12}-androstenol-3β [2] (IX), 17,17-dimethyl-18-nor-$\Delta^{5,12}$-androstadienol-3β [3] (X) and 17,17-dimethyl-18-norandrostanetriol-3β, 12,13 (XI) [2]. Inasmuch as 18-norandrostane compounds have as yet been little studied and spectral data on these compounds are not given in the literature, the infra-red spectra obtained by us for the compounds mentioned are given in Figure 3.

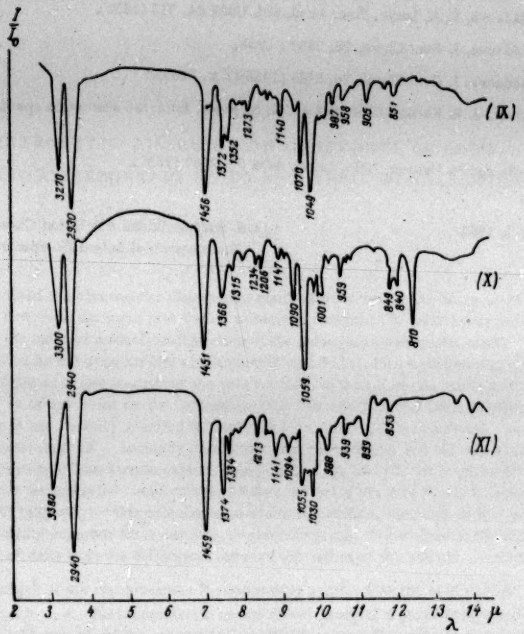


Fig. 3. Infra-red absorption spectra of 17,17-dimethyl-18-nor-Δ^{12}- androstenol-3β (IX), 17,17-dimethyl-18-nor-Δ^{5+12}-androstadienol-3 β (X) and 17,17-dimethyl-18-norandrostanetriol-3 β, 12,13 (XI).

EXPERIMENTAL

The infra-red absorption spectra were obtained using an infra-red recording spectrometer IKS-11 with NaCl prism in the region from 2.5 to 14 μ. All the substances were taken in the crystalline state in the form of a suspension (paste) in vaseline. Substances prepared for elementary analysis were taken for the measurements. In the diagrams, the abscissae give the wavelength (in μ), the ordinates give the transmission (%), and the figures at the minima give the frequencies (in cm^{-1}).

SUMMARY

1. The infra-red spectra of 8 derivatives of the androstane and 18-norandrostane series have been obtained.

2. On the basis of a study of the infra-red spectra it has been shown that the removal of p-toluenesulfonic acid from 3-acetate 17-tosylate of Δ^5-androstenediol-3β, 17β takes place with a retropinacol rearrangement leading predominantly to the formation of the compound with a ditertiary double bond – the acetate of 17-methyl-18-norandrostadienol-3β (II) with an admixture of an isomer – the acetate of 17-methyl-18-nor-Δ^{5+12}-androstadienol-3 β (III) with a secondary-tertiary double bond.

3. The introduction of methyl groups into the 17-position of the androstanol-3β molecule is hardly shown in the infra-red spectra of the corresponding compounds.

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ELECTROLYTIC DISSOCIATION CONSTANTS OF SOME SACCHARODICARBOXYLIC ACIDS AND THEIR MONOLACTONES

L. A. Mai

We have determined the electrolytic dissociation constants of several polyhydroxy-ω-dicarboxylic acids of the sugar series and their monolactones (see Table) in order to examine the relationship between acid strength and structure, and also the stereochemical configuration of the polyhydroxymethylene chain. The dissociation constants were determined by the approximate electrometric method [1], i.e., by measuring the pH of solutions containing a mixture of the acid and its salt (by the measurement of the pH of two neutralization points for the dicarboxylic acids, or of one point for the monolactones). The experimental train consisted of—glass electrode | solution of acid and its salt | saturated KCl solution | saturated calomel electrode; ionic strength of the solutions 0.01-0.03, temperature 25°; accuracy (maximum error) ± 0.05 pK. All the materials studied were crystalline with the exception of the monolactone of mucic acid. pK_1 and pK_2 for D-gluco-D-gulopentahydroxy-pimelic acid (could not be separated) were calculated from the pH of the acid K-salt solution ($pK_1 + pK_2$) and the Bjerrum equation [2] ($pK_2 - pK_1$); this calculation seems to us justified, inasmuch as the values of $pK_2 - pK_1$ calculated using the Bjerrum equation for D-tartaric, D-glucosaccharic, D-mannosaccharic and mucic acids agree within the limits of error with the differences between the values of pK_2 and pK_1 determined experimentally.

1) The acid strength of the monolactones is considerably greater than the acid strength of the corresponding dicarboxylic acids, i. e., the lactonization of one COOH-group of a polyhydroxy-ω-dicarboxylic acid raises considerably the acid strength of the remaining free COOH-group. This phenomenon has already been pointed out for D-glucosaccharic acid by J. Meyer [3] and is an interesting example of the influence of cyclic structure on the acid strength of a substance; in this case the increase in acid strength is undoubtedly caused by the closure of the planar furanyl γ-lactone ring.

Dissociation exponents for some polyhydroxy-ω-dicarboxylic acids and their monolactones

Substance	pK_1	pK_2
Mucic acid*	3.29	4.41
D-Glucosaccharic acid*	3.01	3.94
D-Mannosaccharic acid	2.94	3.88
D-Gluco-D-gulopentahydroxypimelic acid	3.25	4.18
Monolactone of mucic acid	2.72	–
3,6-Monolactone of D-glucosaccharic acid**	2.76	–
1,4-Monolactone of D-glucosaccharic acid	2.72	–
Monolactone of D-gluco-D-gulopentahydroxypimelic acid	2.81	–
Monoethyl ester of mucic acid	3.64	–

* The data from the first conductometric determinations published earlier are [5]; K_1^{25} mucic acid (determined conductometrically) $6.1 \cdot 10^{-4}$ [6]; K_1^{25} D-glucosaccharic acid (determined conductometrically) $1.0 \cdot 10^{-3}$ [3]; Beilstein's collection [vol. III, 577 (1921)] and the Dictionary of Organic Compounds [vol. III, 608 (1949)] give for K_1^{25} the erroneous value $1.0 \cdot 10^{-5}$.

** K^{25} $1.7 \cdot 10^{-3}$ by conductometric method [3].

2) The monoesters of polyhydroxy-ω-dicarboxylic acids obey, at any rate approximately, the "acid ester rule" [4], according to which $K_1 \approx 2K_{\text{acid ester}}$ (K_1/K monoester for the monomethyl ester of D-tartaric acid equals 2.57, for the monoethyl ester of mucic acid 2.24).

3) The sequence of increasing acid strength in the aldohexose series galactose—glucose—mannose preserved also in the ω-dicarboxylic acids of these steric series.

SUMMARY

1. The acid strengths (dissociation constants) have been determined by the approximate electrometric method for D-glucosaccharic, D-mannosaccharic and mucic acids, their mono-γ-lactones, the mono-γ-lactone of D-gluco-D-gulopentahydroxypimelic acid and the monoethyl ester of mucic acid.

2. The acid strength of the mono-γ-lactones studied is considerably greater than the acid strength of the corresponding dicarboxylic acids.

3. The acid strength of the monoesters of polyhydroxy- ω-dicarboxylic acids is lower than the acid strength of the corresponding dicarboxylic acids.

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INNER COMPLEXES OF AZOCOMPOUNDS

IV. THE REACTION OF COPPER SALTS WITH CERTAIN o-HYDROXY- AND o-AMINO-o'-METHYLTHIOAZOCOMPOUNDS

V. I. Mur

In previous communications [1,2] we have described the complexes of copper with o-hydroxy and o-amino-o'-alkoxy azocompounds and indicated the conditions for their mutual interconversion. In the present work it seemed of interest to follow the reaction of copper salts with the corresponding alkylthio azocompounds, as examples of which we chose 1-(o-methylthiobenzeneazo)-2-naphthol, 1-phenyl-3-methyl-4-(o-methylthio benzeneazo)-5-pyrazolone, 1-(o-methylthiobenzeneazo)-2-naphthylamine and 1-phenyl-3-methyl-4-(o-methylthiobenzeneazo)-5-aminopyrazole.

It turned out that o-hydroxy-o'-methylthio azocompounds react with copper salts in alcohol and in aqueous alcohol in the presence of ammonia in the same way as the o-hydroxy-o'alkoxy azocompounds. Thus, in the reaction with cupric chloride in alcohol, complexes with composition 1:1 are formed, with structure (I) analogous to the corresponding complexes of o-hydroxy-o'methoxy azocompounds. In the reaction with tetrammino cupric sulfate in aqueous alcohol, complexes with composition 1:2 (II) are formed. The same 1:2 complexes are formed by the reaction of ammonia or pyridine with the 1:1 complexes (without heating). All the complexes obtained are easily decomposed by mineral acids with the formation of the original o-hydroxy-o'-methylthio azocompounds.

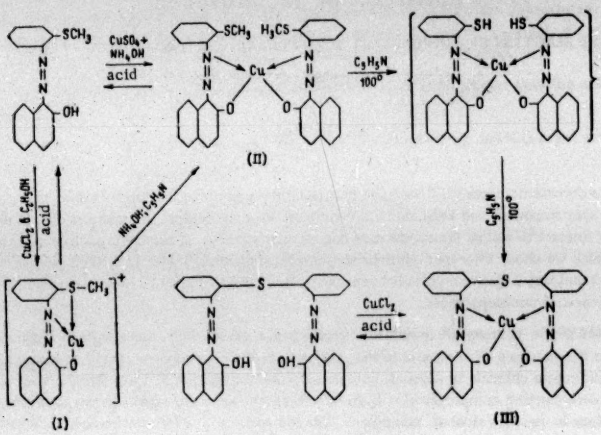
The o-amino-o'-methylthio azocompounds also react with cupric chloride in alcohol with the formation of 1:1 complexes. These substances, however, in contrast to the o-amino-o'-alkoxy azocompounds [2], do not form 1:2 complexes; instead the azocompound is converted into the corresponding triazole.

When one of the o-hydroxy-o'methylthio azocompounds—1-(o-methyl-thiobenzeneazo)-2-naphthol—is heated for a short time with copper sulfate and pyridine, with or without alcohol, at 80 and 100°, i.e., in the conditions under which the o-hydroxy-o'-alkoxy azocompounds are converted into the o,o'-dihydroxy azocompounds, no such change is observed with the thioazocompounds. When the same reagents are heated for longer periods (10, 20, 40 hours), a mixture of copper complexes is formed, and when this is decomposed with sulfuric acid, the original azocompounds are obtained together with greater or lesser amounts depending on the duration of the reaction, of di-o-(2-hydroxy-naphthalene-1-azo)-phenyl sulfide. The formation of a complex of the latter compound with copper is evidently the result of interaction between pyridine and the copper complex of 1-(o-mercaptophenylazo)-2-naphthol, formed initially as an unstable intermediate product of the reaction of 1-(o-methylthiobenzeneazo)-2-naphthol with copper sulfate and pyridine. Evidence for this suggestion is provided by the data [3] on the conversion of o-aminothiophenol into o,o'-diaminodiphenyl sulfide by heating in pyridine. Experimental confirmation of the possibility of converting the copper complex of 1-(o-mercaptophenylazo)-2-naphthol into the copper complex of di-o-(2-hydroxynaphthalene-1-azo)-phenyl sulfide by heating it in pyridine is not possible, inasmuch as a complex of copper and the above thiophenol with the expected composition and structure has not been isolated by us, nor by earlier workers [4] who have tried to prepare it by the reaction of 1-(o-mercaptophenylazo)-2-naphthol with copper sulfate.

Di-o-(2-hydroxynaphthalene-1-azo)-phenyl sulfide and its copper salt were prepared for identification by a supplementary synthesis. The copper salt obtained by the reaction of alcohol solutions of di-o-(2-hydroxy-

naphthalene-1-azo)-phenyl sulfide [4] and cupric chloride has a composition corresponding to the empirical formula $C_{32}H_{30}O_2N_4SCu$; its probable structure may be represented by formula (III).

The observed changes which take place in the reaction of 1-(o-methylthiobenzeneazo)-2-naphthol with copper salts and the changes undergone by the resultant complexes are shown in the diagram.



EXPERIMENTAL

The compounds being studied – o-hydroxy-and o-amino-o'-methylthioazocompounds – were prepared by coupling 2-aminothioanisole with 2-naphthol and 1-phenyl-3-methyl-5-pyrazolone in alkali carbonate medium and with 2-naphthylamine and 1-phenyl-3-methyl-5-aminopyrazole in acetic acid medium and recrystallization from ethyl alcohol. The 2-amino-thioanisole was obtained according to the scheme: o-nitrochlorobenzene → o,o'-dinitrodiphenyl disulfide → o-nitrothiophenol → o-nitrothioanisole → o-aminothioanisole. The first stage was carried out under the conditions used by R. Mohlau [5], the second and third stages were carried out successively without separation of the o-nitrothiophenol, using data provided by the work of K. Brandt [6] for the second stage and of D. Foster [7] for the third stage; the reduction of the nitrocompound to the amino-compound was carried out according to the method of T. Zincke [8]. The substances described in the literature were identified by their melting points, substances not so described – by their nitrogen content.

1-Phenyl-3-methyl-4-(o-methylthiobenzeneazo)-5-pyrazolone: yellow glistening needles, m. p. 148-149°.

Found %: N 17.56. $C_{17}H_{16}ON_4S$. Calculated %: N 17.28.

1-(o-Methylthiobenzeneazo)-2-naphthylamine: red needles, m.p. 143.5-145°.

Found %: N 14.44. $C_{17}H_{15}N_3S$. Calculated %: N 14.33.

1-Phenyl-3-methyl-4-(o-methylthiobenzeneazo)-5-aminopyrazole: yellow needles, m.p. 146-147.5°

Found %: N 21.87. $C_{17}H_{17}N_5S$. Calculated %: N 21.67.

The reaction of the o-hydroxy-and amino-o'-methylthio azocompounds with cupric chloride in alcohol and with tetrammino cupric sulfate in aqueous alcohol was carried out under the same conditions as used earlier for the alkoxy azocompounds [1,2].

The copper salt of 1-(o-methylthiobenzeneazo)-2-naphthol. Salt with composition 1:1. Thin long brown needles (under the microscope), decomposing at 260°.

Found %: N 7.34; Cu 16.05. $C_{17}H_{13}ON_2SClCu$. Calculated %: N 7.14; Cu 16.21.

Salt with composition 1:2. Dark brown compact plates or flat prisms with greenish luster (under the microscope); m.p. 221.5-222.5°

Found %: N 8.78; Cu 9.55. $(C_{17}H_{13}ON_2S)_2Cu$. Calculated %: N 8.62; Cu 9.79.

The copper salt of 1-phenyl-3-methyl-4-(o-methylthiobenzeneazo)-5-pyrazolone. Salt with composition 1:1. Fine long greenish yellow needles (under the microscope); m.p. 265° with decomposition.

Found %: N 12.97; Cu 14.93. $C_{17}H_{15}ON_4SClCu$. Calculated %: N 13.27; Cu 15.06.

Salt with composition 1:2. Dark crystals with blue luster; under the microscope – flat prisms with parallelogram as base; m.p. 208-209°.

Found %: Cu 8.81. $(C_{17}H_{15}ON_4S)_2Cu$. Calculated %: Cu 8.96.

The 1:1 copper salts were converted, by heating with an aqueous solution of ammonia (more rapidly on heating) or pyridine, into the corresponding salts with composition 1:2; copper was found (iodometrically) in the filtrate in amounts corresponding to 1 atom for every 2 molecules of the original 1:1 complex.

When 0.2-0.4 g of each of the above salts was dissolved in 2 ml concentrated sulfuric acid and then diluted with 50 ml water, the original azocompounds separated; the copper was determined quantitatively in the filtrate.

The copper salt of 1-(o-methylthiobenzeneazo)-2-naphthylamine 1:1. Long thin reddish-brown needles (under the microscope); started to melt at 195°, decomposed at 198°.

Found %: N 10.77; Cu 16.11. $C_{17}H_{14}N_3SClCu$. Calculated %: N 10.74; Cu 16.25.

The copper salt of 1-phenyl-3-methyl-4-(o-methlthiobenzeneazo)-5-aminopyrazole of composition 1:1. Light brown needles (under the microscope); started to melt at 209°, decomposed at 225°.

Found %: N 16.39; Cu 15.02. $C_{17}H_{16}N_5SClCu$. Calculated %: N 16.62; Cu 15.10.

2-(o-Methylthiophenyl)-naphtho-1', 2': 4,5-triazole. Colorless prisms (from ethyl alcohol; under the microscope); m.p. 210-211.5°.

Found %: N 14.30. $C_{17}H_{13}N_3$. Calculated %: N 14.43.

The reaction of 1-(o-methylthiobenzeneazo)-2-naphthol with copper sulfate and pyridine. 2 g copper sulfate (pentahydrate) in 50 ml pyridine and 30 ml water was added to 2 g of the azocompound in 200 ml ethyl alcohol and the dark reddish-brown solution obtained was heated under reflux on a boiling water bath for different periods of time according to the experiment (4, 10, 20 and 40 hours in experiments 1, 2, 3 and 4, respectively); in a second series of experiments the alcohol was omitted. When heating was stopped the solution was cooled, poured into 1 liter of water and neutralized with acetic acid. The precipitate which separated, when washed with ammonia solution, water and hot alcohol, contained none of the original azocompound.

1 g of the material obtained was dissolved in 4 ml concentrated sulfuric acid, 50 ml water added, the red precipitate which formed was filtered off, washed with water and alcohol and recrystallized. The chief product isolated after recrystallization of the residue in experiment 1 from ethyl alcohol was 1-(o-methylthiobenzeneazo)-2-naphthol, m.p. 162-163°; in experiment 4 the main product separated by recrystallization of the residue from xylene or chlorobenzene was di-o-(2-hydroxynaphthalene-1-azo)-phenyl sulfide, m.p. 283-285°; both substances were also found in experiments 2 and 3, while experiment 2 had more of the original azocompound than experiment 3. Copper was found in the filtrates.

The copper salt of o-di-(2-hydroxynaphthalene-1-azo)-phenyl sulfide. The original sulfide was prepared according to the scheme: o-nitrochlorobenzene → o,o' dinitrodiphenyl sulfide → o,o'-diaminodiphenyl sulfide → o-di-(2-hydroxynaphthalene-1-azo)-phenyl sulfide; the first two stages were carried out under the conditions used in work by R. Nietzki et al. [9], the third stage according to Burawoy et al., [4]. The copper salt was obtained by mixing alcohol solutions of the sulfide and cupric chloride, then diluting with water and washing the brown precipitate obtained with aqueous ammonia solution, water and hot alcohol.

Found %: N 9.06; S 5.40; Cu 10.67. $C_{22}H_{16}O_2N_4SCu$. Calculated %: N 9.53; S 5.45; Cu 10.82.

SUMMARY

1. The reaction of o-hydroxy-and o-amino-o'-methylthio azocampounds with copper salts has been carried out and certain properties of the copper complexes thus obtained have been studied.

2. The thioazocompounds obtained by coupling 2-aminothioanisole with 2-naphthol, 1-phenyl-3-methyl-5-pyrazolone, 2-naphthylamine and 1-phenyl-3-methyl-5-aminopyrazole, their copper salts with composition 1:1 and 1:2, and 2-(o-methylthiophenyl)-naphtho-1', 2': 4, 5-triazole have been prepared.

3. It has been shown that on prolonged heating of 1-(o-methylthiobenzeneazo)-2-naphthol with copper sulfate and pyridine, the copper salt of o-di-(2-hydroxynaphthalene-1-azo)-phenyl sulfide with composition 1:1 is obtained.

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THE REACTION OF TETRAPHENYLTIN WITH ORGANIC ACIDS

M. M. Koton

It has been pointed out in a recent article [1] that tetraethyltin, in its reactions with organic acids, phenols and mercaptans, splits off one ethyl group with the formation of the corresponding triethyltin derivatives. It had been shown earlier by us that in contrast to the alkyl derivatives, tetraphenyltin does not react with pyrogallol at 130° [2] and reacts with phenols and mercaptans only at 150° with complete removal of all the phenyl groups as benzene and the formation of the corresponding tin aryloxides and mercaptides [3]. The reaction of tetraphenyltin with thiosalicylic acid at 130° leads to the formation of benzene and the compound $OSnOCOC_6H_4S$ [4]. Up to the present time the action of organic acids on tetraphenyltin has remained unknown, and there are no notices of reactions of this type in the literature. We have studied the reaction of tetraphenyltin with formic and acetic acids at temperatures from 50 to 125°.

The studies carried out have shown that tetraphenyltin is very stable toward organic acids at temperatures below 100°. At 100-125° tetraphenyltin splits off the phenyl radicals completely, with the formation of benzene and the corresponding tin salts, according to the general equation:

$$(C_6H_5)_4Sn + 4RCOOH \rightarrow 4C_6H_6 + Sn(OCOR)_4.$$

In the reaction of tetraphenyltin with formic acid (Table 1) at 100-115°, the tin tetraformate formed is immediately converted to a basic salt with composition $(HCOO)Sn(OH)_3$. In the reaction of tetraphenyltin with acetic acid (Table 2) at 125°, the tin tetraacetate formed is also converted to a basic salt, with approximate composition $(CH_3COO)Sn(O)OH$.

TABLE 1

Temperature	Duration of experiment (in hours)	$(HCOO)Sn(OH)_3$ obtained in g	$(C_6H_5)_4Sn$ residue in g
50°	1	0	0,290
75	1	0	0,295
90	1	0,02	0,280
100	0,5	0,03	0,270
100	1	0,15	0
115	1	0,14	0

The chlorides of organic acids react more vigorously with tetraphenyltin than the parent acids. We have shown that acetyl chloride reacts with tetraphenyltin even at 50° with the formation of $(C_6H_5)_2SnCl_2$, and at 100-130° complete decomposition of the tetraphenyltin takes place with the formation of acetophenone and stannic chloride.

TABLE 2

Temperature	Duration of experiment (hrs)	$(CH_3COO)_3Sn(O)OH$ obtained (in g)	$(C_6H_5)_4Sn$ residue (in g)
75	1	0	0.295
100	1	0	0.290
100	2	0	0.280
125	1	0.06	0.090
125	2	0.11	0.0

EXPERIMENTAL

All the experiments were carried out in sealed glass ampoules, heated in a thermostat at a closely regulated temperature; 1 ml of organic acid or acetyl chloride was taken for 0.3 g tetraphenyltin.

All the reactions with the organic acids were carried out at 50, 75, 100, 115 and 125°. After heating, the contents of the ampoule were treated with absolute solvents (xylene, benzene, ether), the insoluble residue dried in a vacuum desiccator to constant weight and analyzed for its tin content (Tables 1 and 2). Special tests were carried out to determine the composition of the products obtained.

Tetraphenyltin and formic acid. 1 g tetraphenyltin and 1.5 ml anhydrous formic acid were heated for 3 hours at 100° and then the benzene and excess formic acid were distilled from the ampoule. 0.85 ml benzene was collected (complete removal of all the phenyl groups should give 0.91 ml benzene). After treatment with solvents, 0.47 g of a white residue, which did not melt below 250°, was obtained in the ampoule. The substance was dissolved by heating in 50% alkali solution and recovered by acidification; on reaction with hydrogen sulfide a yellow precipitate of SnS_2 was obtained.

Found %: Sn 54.87. $(HCOO)Sn(OH)_3$. Calculated %: Sn 55.35.

Tetraphenyltin and acetic acid. 1 g tetraphenyltin and 1.5 ml anhydrous acetic acid were heated for 2 hours at 125°. 0.75 ml benzene were collected (complete removal of all the phenyl groups should give 0.82 ml). After treatment with solvents, 0.45 g of insoluble material, which did not melt below 260°, was obtained.

Found %: Sn 56.39. $(CH_3COO)Sn(O)OH$. Calculated %: Sn 56.24.

Tetraphenyltin and acetyl chloride. Tests were carried out at 15, 50, 100 and 130°. After heating for 1 hour at 50°, the ether solution yielded fine hygroscopic crystals of dichlorodiphenyltin with m.p. 36-41° (literature data 42°). After heating for 2-3 hours at 100 and 130° the formation of stannic chloride was observed, as proved by the formation of a yellow precipitate of SnS_2 on treatment with hydrogen sulfide. The presence of acetophenone was proved by the well known qualitative tests with sodium nitroprusside and m-dinitrobenzene.

SUMMARY

1. Tetraphenyltin reacts with organic acids (formic and acetic) at 100-125° with complete removal of all the phenyl groups and the formation of benzene and basic Sn^{IV} salts.

2. Tetraphenyltin reacts with acetyl chloride at 50° with the formation of $(C_6H_5)_2SnCl_2$ and at 100-130° with the formation of $SnCl_4$ and acetophenone.

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USSR Academy of Sciences

* T.P. = C. B. Translation pagination.

THE HALOGENOARYLATION OF UNSATURATED COMPOUNDS WITH AROMATIC DIAZOCOMPOUNDS

II. ACRYLONITRILE IN HALOGENOARYLATION

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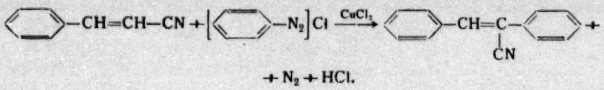
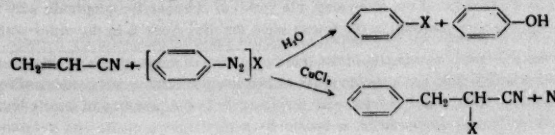
As is known, diazonium salts in the presence of cupric chloride in acetone solution exhibit the property of reacting with unsaturated compounds, losing nitrogen in the process. The halogenoaryl derivatives formed have varying stability; in some cases they cannot be isolated, since they undergo further changes during the reaction which finally result in the removal of the hydrogen halide. This reaction, which was discovered by Meerwein [1], is a convenient method for the arylation of unsaturated compounds, and many examples of its use are known at the present time. Thus, the reaction of benzenediazonium chloride with cinnamonitrile in acetone solution in the presence of cupric chloride leads to the formation of α,β-diphenylacrylonitrile in 70% yield [1]:



$$+ N_2 + HCl.$$

The halogenoarylation of divinyl (butadiene) has been described in a previous communication [2]. Acrylonitrile also undergoes a similar reaction giving α-chloro-β-arylpropionitrile [3]. Brunner and Perger [4] have used this reaction for the synthesis of various chloroarylpropionitriles with substituents in the nucleus. Muller [5] and later Malinowsky [6] simplified the reaction and carried it out without sodium acetate in a medium of hydrochloric acid and aqueous acetone; the yields of chloroarylpropionitriles obtained in this way were not lowered.

We have undertaken a systematic study of this reaction. The reaction was carried out in the same way in all cases: the solution of the diazonium salt was added to a mixture of acrylonitrile and cupric chloride (or bromide) in acetone at such a rate that the temperature did not exceed that at which decomposition of the diazonium salt and evolution of nitrogen took place. At the end of the process and after the usual treatment of the reaction mass, the various halogenobenzenes and phenols were isolated in all cases in addition to the chief product of the reaction – the halogenoarylpropionitrile.



where x = Cl, Br.

The proportions of the reaction products obtained are given in Table 1. The yields are calculated from the original aromatic amine.

TABLE 1

Halogenoarylation of Acrylonitrile with Aryldiazonium Salts

Diazonium salt	Reaction temperature	Yield (%)		
		halogeno-arylpropio-nitrile	halogeno-benzene	phenol
Benzenediazonium chloride	7°	42.5 *	35	Traces
p-Nitrobenzenediazonium chloride	18	96.5	—	—
m-Nitrobenzenediazonium chloride	10	50.0	—	—
o-Nitrobenzenediazonium chloride	21	45.0	30	—
Benzenediazonium chloride	21	32.0	33.5	10.0
p-Toluenediazonium bromide	16	30.2	32.5	—
p-Nitrobenzenediazonium bromide	—6	54.0	25.0	—

In addition to the substances mentioned, small quantities of chloro- and bromoacetone were formed in the reaction.

Increase in temperature decreases the yield of halogenoarylpropionitrile and increases the yield of halogenobenzene and phenol. For example, in the reaction of acrylonitrile with benzenediazonium chloride at 7° the yield of α-chloro-β-phenylpropionitrile was 40%; at 20° the yield was lowered to 18-20%, while the yield of chlorobenzene was correspondingly increased.

The presence of cupric chloride or bromide is an essential condition for halogenoarylation. Attempts to carry out the halogenoarylation of acrylonitrile in the presence of Cu_2Cl_2, $SnCl_2$, $CoCl_2$, $MnCl_2$, $NiCl_2$, $CdCl_2$, $ZnCl_2$ and $AlCl_3$ gave no positive results. In the case where the double salt $p\text{-}NO_2C_6H_4N_2Cl \cdot FeCl_3$ was used, the formation of α-chloro-β-(4-nitrophenyl)-propionitrile in 11% yield was observed. It also did not prove possible to carry out arylhalogenation by the reaction of acrylonitrile with p-nitrobenzenediazonium chloride under ultraviolet light; instead of the expected product, a colored tarry material was obtained.

In this connection it is interesting to note that in the presence of boron trifluoride, acrylonitrile reacts with benzenediazonium salts in an entirely different manner. As L. G. Makarova and A. N. Nesmeyanov [7] have recently found, the end product of the decomposition of diazonium borofluoride in acrylonitrile is not the halogenoarylpropionitrile but acrylanilide.

The influence of addition of sodium acetate and calcium oxide on the process of halogenoarylation has been studied taking the reaction of benzenediazonium chloride with acrylonitrile as an example. The results are given in Table 2. As can be seen from the data in this Table, when the reaction is carried out in the presence of sodium acetate the yield of the chief product is increased and the formation of the phenol is prevented; calcium oxide does not favor the production of α-chloro-β-phenylpropionitrile.

The presence of negative substituents in the nucleus leads to an increased yield of chloroarylpropionitrile. Thus, the reaction of p-,m-and o-nitrobenzenediazonium chlorides gave yields of the corresponding chloronitrophenylpropionitriles which were higher than the yield of chlorophenylpropionitrile from benzenediazonium chloride. Depending on the position of the nitrogroup, the yields of chloroarylpropionitrile vary from the greatest when the nitrogroup is in the para-position, to the lowest when the nitrogroup is in the ortho-position.

We have studied a number of examples of the bromoarylation of acrylonitrile (Table 1), which have not been described before. Starting from the hydrobromides of aniline, p-toluidine and p-nitroaniline, we prepared the corresponding diazonium salts, which reacted with acrylonitrile in the presence of cupric bromide to give respectively: α-bromo-β-phenyl-propionitrile, α-bromo-β-(p-tolyl)-propionitrile and α-bromo-β-(4-nitrophenyl)-propionitrile. It should be noted that the yields of bromarylpropionitriles are lower than those of the corresponding chloro derivatives.

TABLE 2

The Influence of Added Substances on the Yield of α-Chloro-β-phenylpropionitrile

Added substance	Reaction temperatures	Yield (%)		
		α-chloro-β-phenylpropionitrile	chlorobenzene	phenol
No added substance	7°	21.7	1.96	13.8
Sodium acetate	5–7	42.5	35.0	traces
Calcium oxide	7–10	30.0	traces	5.0

Although the reaction of acrylonitrile and o-nitrobenzenediazonium chloride has been described earlier [6], the α-chloro-β-(2-nitrophenyl)-propionitrile was not separated and characterized. This nitrile was obtained by us in 45% yield and its physico-chemical characteristics are given.

EXPERIMENTAL

The aromatic amines were diazotized by the generally adopted method. The quantities of material were taken according to the calculation: 5 mole hydrochloric acid (d 1.19) or 3 mole hydrobromic acid (d 1.38) to 1 mole of amine. For the diazotization, the sodium nitrite was dissolved in the minimum amount of water.

1. α-Chloro-β-phenylpropionitrile. 10.6 g acrylonitrile, 100 ml acetone, 5 g cupric chloride and 27 g crystalline sodium acetate were placed in a three-necked flask fitted with stirrer, dropping funnel and thermometer, the mixture was cooled to 5°, and a solution of benzenediazonium chloride, prepared by diazotizing 19.6 g aniline, was added dropwise. Vigorous evolution of nitrogen began soon after the diazonium salt solution had been added, and was complete 1.5–2 hours after the diazo solution had been added. The flask was cooled during the reaction, so that the temperature did not rise above 12°. When the evolution of nitrogen was complete, the reaction mass was diluted with water and the oil which separated was extracted with ether. The ether extract was washed with sodium carbonate solution and then with water, and dried with calcium chloride. After distillation of the ether and acetone the residue was vacuum distilled: 1st fraction – chlorobenzene, 8.0 g (35% calculated from the amine); 2nd fraction – α-chloro-β-phenylpropionitrile, b.p. 135-140° at 15 mm, m.p. 18-20°. Literature data [4]: b.p. 135-140° at 15 mm, m.p. 19-21°. 14 g (42.5%) of substance was obtained. In addition, traces of phenol were distilled. A tarry residue containing nitrogen was left in the flask after the distillation. When the reaction was carried out with the addition of calcium oxide, more vigorous cooling was required.

2. α-Chloro-β-(4-nitrophenyl)-propionitrile. 42 g of crude product was obtained, at 18°, by the method described above, from 10.6 g acrylonitrile, 100 ml acetone, 5 g cupric chloride and 5 g cupric chloride and p-nitrobenzenediazonium chloride prepared from 27.5 g p-nitroaniline. Recrystallization from methyl alcohol yielded 40.5 g (96.5%) of pure substance, m.p. 110-111°. Literature data [5]: m.p. 110-112°.

3. α-Chloro-β-(3-nitrophenyl)-propionitrile. 21 g (50%) α-chloro-β-(3-nitrophenyl)-propionitrile, m.p. 83-84°, was obtained from the same quantities of acrylonitrile and m-nitroaniline. Literature data [3]: m.p. 83-84°.

4. α-Chloro-β-(2-nitrophenyl)-propionitrile was prepared by the method described above from the o-nitrobenzenediazonium salt prepared from 13.8 g aniline, with 6 g acrylonitrile in 100 ml acetone in the presence of 5 g cupric chloride at 21°. Yield of nitrile 9.5 g (45%). B. p. 166-168° at 4 mm, n_D^{20} 1.5672, d_4^{20} 1.336, MR_D 51.50; calc. 51.06.

5. α-Chloro-β-(4-nitrophenyl)-propionitrile from the double salt $p\text{-}NO_2C_6H_4N_2Cl \cdot FeCl_3$, and acrylonitrile. 60 g (70%) of the complex salt $p\text{-}NO_2C_6H_4N_2Cl \cdot FeCl_3$ was obtained from 27.5 g p-nitroaniline according to the method described in [8]. The salt was purified by reprecipitation from acetone solution with dry ether [9]. M. p. 91-92° (with decomp.). 28 g of the complex salt was mixed with a solution of 5.5 g acrylonitrile in 100 ml acetone. On the addition of 10 ml water, a considerable evolution of nitrogen took place and continued at 20-30°. Treatment of the reaction mixture yielded 2 g α-chloro-β-(4-nitrophenyl)-propionitrile, m.p. 110° and 10.7 g (85%) p-chloronitrobenzene, m.p. 83°.

6. α-Bromo-β-phenylpropionitrile. 10.3 g acrylonitrile in 100 ml acetone, 5 g cupric bromide and benzenediazonium bromide prepared from 19.6 g aniline were taken for the reaction. The nitrogen was evolved at 21°. After the usual treatment the residue was vacuum distilled: 1st fraction – bromobenzene, 10.5 g (33.5%), b.p. 156.2°, n_D^{20} 1.5602; 2nd fraction – α-bromo-β-phenylpropionitrile, 13.2 g (32%), b.p. 114-114.5° at 3 mm, n_D^{20} 1.5719, d_4^{20} 1.380, MR_D 47.74; calc. 50.01. Literature data [4]: b.p. 143-145° at 15 mm, m.p. 27-28°. After several distillations the constants of the material did not change; the substance, however, obviously contained an admixture of an unsaturated substance (decolorized potassium permanganate solution and bromine water).

Found %: N 7.43, 7.47. C_9H_8NBr. Calculated %: N 6.67.

7. α-Bromo-β-(p-tolyl)-propionitrile. 12 g acrylonitrile in 100 ml acetone, 5 g cupric bromide and p-toluenediazonium bromide prepared from 19 g p-toluidine were treated as described above, giving: p-bromotoluene 10 g (32.5%), b.p. 56-62° at 6 mm, m.p. 28-28.5° (literature data: b.p. 184-185°, m.p. 28.5°) and α-bromo-β-(p-tolyl)-propionitrile, 12 g (30.2 %), b.p. 121-121.5° at 2 mm, n_D^{20} 1.5620, d_4^{20} 1.345, MR_D 54.10; calc. 52.27. The constants of the substance did not chage after several distillations; there were present however, traces of an unsaturated compound (a sample of the material decolorized potassium permanganate solution and bromine water).

Found %: N 6.75, 6.86. $C_{10}H_{10}NBr$. Calculated %: N 6.25.

8. α-Bromo-β-(4-nitrophenyl)-propionitrile. 5.3 g acrylonitrile and p-nitrobenzenediazonium bromide prepared from 13.5 g p-nitroaniline yielded at −10°: p-bromonitrobenzene, 5.1 g (25 %), b.p. 120-130° at 6 mm, m.p. 127°. Literature data: m.p. 126-127° α-bromo-β-(4-nitrophenyl)-propionitrile, b.p. 192-194° at 2 mm, m.p. 98.5-99° after recrystallization from methyl alcohol. Yield 13.5 g (54%).

Found %: N 11.17. $C_9H_7O_2NBr$. Calculated %: N 10.98.

SUMMARY

1. Acrylonitrile reacts with diazonium salts in acetone solution in the presence of cupric halides; in addition to the chief reaction products – α-halogeno-β-arylpropionitriles – aryl halides and phenols are formed. The proportions of the substances formed depend to a great extent on the temperature conditions of the reaction.

2. The chlorides of $Cu, Sn, Co, Mn^{++}, Ni^{++}, Cd^{++}, Zn^{++}, Al^{+++}$ have been tested as catalysts for the reaction. Only cupric halides catalyze the reaction.

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SPECIOSINE – A NEW ALKALOID FROM COLCHICUM SPECIOSUM STEV.

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With a view to obtaining supplies of colchamine [1] we treated fresh corms of Colchicum speciosum Stev. collected in 1954.

The extractive material from the juice of the corms was obtained using the method of A. L. Kolesnikov, D. P. Snegirev and B. T. Pavlov [2]. On further study it turned out that the basic fraction contained, in addition to colchamine, a relatively large amount of a new alkaloid. The concentration of the latter in the raw material amounted to 0.025%, with an approximately equal concentration of colchamine. At the same time colchicine was isolated from the neutral fraction in an amount 0.12% of the weight of the raw material.

The high concentration of a new alkaloid was unexpected, since in work on corms gathered at the same period of plant vegetation in 1952 and 1953*, this material was obtained only in 1953 and then in an amount less than 0.001% of the weight of the raw material treated.

The new alkaloid, for which we suggest the name "speciosine", was separated from colchamine by splitting the mixture of bases according to basic strength. The characterization of speciosine was very complicated, since its crystalline salts could not be obtained. Speciosine does not form salts with organic acids. The individuality of speciosine was confirmed by chromatography.

The composition of speciosine is $C_{23}H_{31}O_6N$, m.p. 209-211°, $[\alpha]_D^{20} - 21.1°$. The presence of one hydroxyl and four methoxy groups was established by analysis. The nitrogen is evidently tertiary, since speciosine forms a methiodide in low yield. The nitrogen is unlikely to be amide nitrogen from the basic properties of speciosine.

We have to express gratitude to L. M. Utkin for his constant interest in the work.

EXPERIMENTAL

Isolation of speciosine.** Fresh corms from Sochi were gathered at the end of September and beginning of October in the locality of Kepsh-Chvizhepse in the plant's flowering period. 3-4 weeks after being gathered, 6 kg of these corms were finely chopped. The juice was pressed from the mass obtained (2.9 liters). The residue was washed twice with 2 liter portions of water and the liquid pressed out again. The liquid obtained (total volume 7.3 liters) was treated three times with chloroform. The combined chloroform extracts (14-15 liters) were evaporated to a volume of 190-200 ml, extracted 3 times with 25 ml portions of 10% H_2SO_4 and washed with 10 ml water. The acid extracts and the wash water were combined and made alkaline with 100 ml 10% NaOH. The alkaloids which precipitated were exhaustively extracted with chloroform. The extract was dried sodium sulfate. The tarry residue remaining after distilling off the chloroform weighed 4.96 g. The residue was dissolved in 10 ml acetone. After some time 1.39 g of impure speciosine with m.p. 194-196° separated.

* In 1953 the material was given by the expedition from the S. Ordzhonikidze All-Union Chemical and Pharmaceutical Scientific Research Institute working under the direction of P. S. Massagetov, and in 1952 by Sh. A. Karapetyan.

** In conjunction with M. S. Borodach.

The mother liquor yielded 1.74 g impure colchamine. 0.2 g of speciosine was isolated from the latter by separation according to basic strength. The initial chloroform extract which remained after extraction of the alkaloids with acid, yielded approximately 0.3 g speciosine and 7.4 g impure colchicine after a fairly lengthy treatment.

Speciosine. 9.28 g speciosine was fractionated according to basic strength. 7.55 g speciosine with m.p. 207-210° after recrystallization from ethyl acetate was isolated from the solution with acid reaction to congo red or litmus. 0.34 g of colchamine was isolated from the fraction obtained after the appearance of an alkaline reaction to bromothymol blue.

The speciosine obtained was dissolved in 300 ml acetone and the solution evaporated to a volume of 80 ml. On cooling, compact clusters of prismatic crystals appeared, which were removed with difficulty from the walls of the flask. Weight of recrystallized pale yellow material 6.49 g, m.p. 209-211° (the melting point did not change on repeated recrystallization from benzene and acetone). The individual nature of the substance was confirmed by chromatography on alumina and on paper. Modified Dragendorf reagent was used to develop the chromatogram on the paper.

$[\alpha]_D^{20} -21.2°$ (c 1.752, chloroform).

Found %: C 70.42; H 6.46; N 3.03; OH 2.76; OCH_3 25.22. M 446 (by Rast's method).
$C_{28}H_{31}O_6N$. Calculated %: C 70.39; H 6.35; N 2.93; OH 3.56; $4OCH_3$ 25.99. M 477.25.

Speciosine does not dissolve in water, dissolves with difficulty in ether and benzene, somewhat more readily in acetone and alcohol, and easily in chloroform. Speciosine dissolves in dilute acids, but does not dissolve in alkali. Alcohol or acetone solutions of speciosine show a neutral reaction to litmus.

Speciosine gives the characteristic reaction of alkaloids with silicotungstic acid. In this it differs from colchicine, since in the case of colchicine the characteristic precipitate disappears on shaking with chloroform. Speciosine gives no green coloration with ferric chloride in the cold.

SUMMARY

A new alkaloid, to which the name "speciosine" has been given, has been isolated from colchicum speciosum Stev.

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THE STUDY OF PLANT ALKALOIDS OF THE ELAEAGNACEAE FAMILY

THE ISOLATION OF TETRAHYDROHARMOL AND N-METHYLTETRAHYDROHARMOL FROM THE BARK OF ELAEAGNUS ANGUSTIFOLIA L.

T. F. Platonova, A. D. Kuzovkov and P. S. Massagetov

Elaeagnus angustifolia – the narrow-leaved oleaster, is widely distributed in the wild state in the USSR. In Central Asia this plant is found in the form of trees and large bushes in dense thickets near rivers. The material studied was gathered in Kazakhstan in the lower reaches of the river Chu. The present work is a continuation of studies begun earlier on the plant alkaloids of the oleaster family [1].

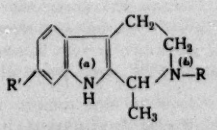
The bark of the Elaeagnus angustifolia on extraction with alcohol, yielded a total basic fraction (0.2% of the weight of dry bark), in which paper chromatography revealed the presence of three alkaloids with R_f values 0.36, 0.47, 0.58. These alkaloids, which are denoted below as (I), (II) and (III), were separated by making use of the varying solubility of the bases and their salts.

Alkaloid (I) has a composition corresponding to the formula $C_{12}H_{14}ON_2$, and its ultraviolet spectrum (Figure 1) resembles that of tetrahydroharmine [2]; the infra-red spectrum (Figure 2) contains the OH- and NH-group bands (2.9, 3.0, 3.8 μ) in the 3μ region. The base possesses phenolic properties. These data show that the molecule of alkaloid (I) is based on the tetrahydroharman nucleus and contains a phenolic hydroxyl group in the benzene nucleus. With the idea that alkaloid (I) might be identical with tetrahydroharmol, which has not yet been described in the literature, we reduced harmol with sodium in anhydrous alcohol. The material thus obtained proved indeed to be identical with alkaloid (I), thus, establishing the structure of the latter.

Alkaloid (II) has the composition $C_{13}H_{16}ON_2$, differing from that of alkaloid (I) in the presence of a CH_2 group. Alkaloid (II) contains the NCH_3 group and shows phenolic properties. On methylation of tetrahydroharmol with methyl iodide, a mixture of products is formed, in which the presence of alkaloid (II) is established by paper chromatography. From this, alkaloid (II) proves to be N-methyltetrahydroharmol. Inasmuch as the alkylation of indole nitrogen is difficult, it may be assumed that the methyl group in alkaloid (II) is found on the piperidine nitrogen.

Alkaloid (III) was identified as eleagnine, which was separated earlier by one of us from Elaeagnus angustifolia and is tetrahydroharman, as was proved by G. P. Menshikov and coworkers [1].

The concentration of alkaloids (I), (II) and (III) in the dry bark are 0.05, 0.001 and 0.1% respectively.



(I) R=H, R'=OH,
(II) R=CH3, R'=OH,
(III) R=R'=H.

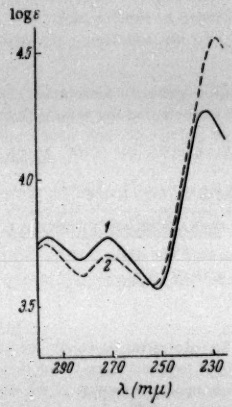


Fig. 1. Ultraviolet absorption spectra in alcohol.
1) Alkaloid (I), 2) tetrahydroharmine.

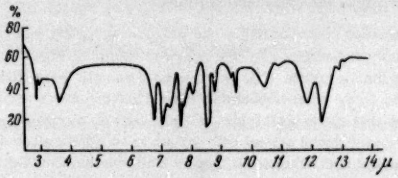


Fig. 2. Infra-red absorption spectrum (in vaseline) of tetrahydroharmol.

EXPERIMENTAL

Isolation of alkaloids. 83 g of finely chopped bark was extracted with isopropyl alcohol containing 1% CH_3COOH. The extract was diluted with twice the volume of water and evaporated in vacuo to a volume of approximately 30 liters. The tar which separated contained no alkaloids and was filtered off. The filtrate was made alkaline with 25% NH_4OH; no individual substances could be separated from the flaky precipitate thus obtained. The aqueous mother liquor was extracted with ether. The extract was treated three times with 10% H_2SO_4. The sulfuric acid solution was made alkaline with 25% NH_4OH in the presence of ether, giving 51 g of a crystalline precipitate (fraction a). The filtrate was exhaustively extracted with ether; the uncrystallized residue (fraction b) weighed 112 g. Three bases with R_f 0.36, 0.47, 0.58 were shown to be present in fractions a and b by chromatography on paper No. 4 (solvent—upper phase of mixture butanol: water: acetic acid in the ratio 50:50:1, time approximately 16 hours, temperature 18-19°, development with iodine vapor).

Treatment of fraction a. 51 g of the mixture of bases was extracted with two 150 ml portions of boiling methanol. The alcohol-insoluble residue yielded the hydrochloride of alkaloid (I), 20 g of which were recovered after recrystallization from a mixture of methanol and ether, m.p. 235°; readily soluble in water, less readily in alcohol.

Found %: C 60.31; H 6.68; N 11.58; Cl 14.72. $C_{13}H_{14}ON_2 \cdot HCl$ Calculated %: C 60.31; H 6.33; N 11.73; Cl 14.85.

Alkaloid (I) was obtained by heating an aqueous solution of the hydrochloride to 50° and making alkaline with 10% NH_4OH. The base had m.p. 256°, R_f 0.36; insoluble in water, dichloroethane, acetone and ether, soluble in aqueous alkali.

Found %: C 71.41; H 7.04; N 13.80. $C_{13}H_{14}ON_2$. Calculated %: C 71.27; H 6.97; N 13.85.

A further 20 g of impure alkaloid (I) was isolated from the mother liquors.

Treatment of fraction b. 112 g of the mixture of bases was dissolved in 500 ml 10% H_2SO_4, and on the next day the precipitate (70 g) of the crystalline alkaloid (III) sulfate was filtered off. The base obtained from the sulfate melted at 178-180°, R_f 0.58. A mixture with eleagnine melted at 178-180°, R_f eleagnine 0.58.

The mother liquor from the eleagnine sulfate yielded a mixture of bases from which 3.5 g alkaloid (I) was isolated by grinding up with acetone. The residue of bases was separated into a phenolic and non-phenolic part by extracting the phenolic part from a chloroform solution of the bases with 5% NaOH. 10 g of eleagnine was isolated as the sulfate from the non-phenolic part.

The phenolic bases (5 g) were dissolved in 5% HCl, after which 0.9 g of the hydrochloride of alkaloid (II) precipitated, m.p. 274-275° (from water).

Found %: C 57.59; H 7.12; N 10.85; Cl 13.08. $C_{13}H_{16}ON_2 \cdot HCl \cdot H_2O$. Calculated %: C 57.66; H 7.07; N 10.33; Cl 13.09.

The alkaloid (II) with m.p. 268-270° (from alcohol), R_f 0.47, was obtained by making an aqueous solution of the hydrochloride alkaline with ammonia.

Found %: C 72.26; H 7.50; N 12.45; NCH_3 7.95. $C_{13}H_{16}ON_2$. Calculated %: C 72.20; H 7.47; N 12.96; NCH_3 13.43.

The reduction of harmol to tetrahydroharmol. 6 g sodium was added to a boiling solution of 1 g harmol in 70 ml anhydrous alcohol. When the sodium had dissolved, the reaction mass was cooled in a current of N_2 and acidified with 18% HCl. The precipitate was separated with sodium chloride and the alcohol distilled off in vacuo. The residue was dissolved in water, the solution made alkaline with 25% NH_4OH in the presence of ether; the dark crystalline precipitate which was obtained was dissolved in 5 ml methanol. The addition of an alcohol solution of HCl precipitated 0.4 g of hydrochloride, m.p. 235° (from a mixture of alcohol and ether). The base, separated from the hydrochloride, melted at 256°, R_f 0.36. A mixture with alkaloid (I) had m.p. 256°. The infra-red spectrum of the material synthesized coincided completely with the spectrum of alkaloid (I).

The methylation of tetrahydroharmol. 1 g tetrahydroharmol, 1 ml CH_3I and 20 ml methanol were boiled for 3 hours and the residue remaining after evaporation was dissolved in water. The solution was made alkaline with 25% NH_4OH and extracted with chloroform. The extract was evaporated and the mixture of bases chromatographed on paper as described above. The spots obtained had R_f values: 0.36 (unchanged tetrahydroharmol), 0.47 (N-methyltetrahydroharmol: the position of the spot was the same as that of the spot of alkaloid II), 0.61 (apparently dimethyltetrahydroharmol)

SUMMARY

Two new alkaloids – tetrahydroharmol and N-methyltetrahydroharmol – have been isolated from the bark Elaeagnus angustifolia, in addition to eleagnine, which has been separated earlier.

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* T. p. = C. B. Translation pagination.

IN MEMORIAM A. A. STREPIKHEEV

The death took place suddenly on July 11, 1955 of Professor Aleksandr Aleksandrovich Strepikheev, Doctor of Chemical Sciences.

A. A. Strepikheev was born in Moscow on April 16, 1912. In 1928 he left secondary school and in the same year entered the chemistry faculty in the Moscow Higher Technical Institute, later reorganized as the Voroshilov Military Chemical Academy, after which he was sent to work in the Artificial Fiber Scientific Research Institute. Here A. A. worked on the solution of a series of extremely important problems connected with production of acetate rayon. This work later provided the material for his higher degree thesis.

A. A. Strepikheev began systematic scientific studies in the field of high-molecular compound chemistry in 1939 and continued these without interruption until the last days of his life. He undertook studies in the field of polyamide resin and polyurethane synthesis and on certain problems connected with the polymerization of saturated compounds. In 1941 he published a survey "Synthetic Fibers and their Preparation". During the Second World War he carried out a number of tasks connected with the preparation and use of mixtures which formed the basis for synthetic resins of importance in defence. From 1948 to 1953 A. A. was scientific director of the All-Union Artificial Fiber Scientific Research Institute (VNIIV). Here he put much work and creative energy into the creation, testing and introduction of new technological processes for the production of artificial and synthetic fibers. He took part in the working out of an efficient new method for preparing viscose solution and a continuous method of molding and finishing viscose cord. The introduction of new technological processes has greatly raised the technical level of the artificial fiber industry.

In all his creative work A. A. Strepikheev was closely connected with the work of industry, had its interests at heart, and deservedly earned the deep respect of the engineering and technical workers in industry. In 1950 a new method was successfully worked out under his direction for the preparation of hydrated cellulose fibers from solutions of cellulose in aqueous solutions of quaternary ammonium bases. When the problems of the technical process and the regeneration of the bases have been successfully solved, this method for preparing hydrated cellulose fibers may have considerable advantages over all methods of preparing cellulose fibers known at the present time. In this method of preparing the fiber the technological process is considerably simplified and the problems of rendering the production safe are solved completely. At the present time, films and fibers with satisfactory physico-chemical properties have been prepared on a pilot-plant scale.

Until recently it was considered that quaternary ammonium bases dissolved only cellulose with comparatively low molecular weight. The work of A. A. Strepikheev and coworkers has shown that the difficulty of dissolving cellulose is to a large extent caused by impurities present

in the bases. Aqueous solutions of the pure bases dissolve cellulose of any molecular weight with the formation of transparent uniform solutions.

Since 1949 a laboratory for organic synthesis founded by A. A. has been in existence in the VNIIV, where work has developed successfully on the synthesis of new monomers for the preparation of fiber-forming polymers and on the solution of problems related to the interconversion of rings and linear polymers.

In the very first years of the laboratory's work, studies in the fields indicated led to valuable practical results. A method was proposed for the preparation of a new fiber-forming polyamide, while a solution was also found to a number of practical problems in connection with the production of capron fiber. In 1950, A. A., together with other scientists and industrial workers was awarded a Stalin prize for overcoming the problems associated with the production of capron fiber.

A. A. Strepikheev created and successfully developed an entirely new scientific field—the study of the interconversion of rings and linear polymers. This reaction is one of the least studied in high-molecular compound synthesis, in spite of the fact that it has recently acquired considerable technological significance and that its role in biological processes is becoming more evident. In a dissertation for his doctorate, which A. A. presented in 1950, the general lines of the theory of the interconversion of rings and linear polymers are laid down and a thermodynamic treatment of this reaction is given, which allows the direction and the final result of the reaction of ring polymerization under different conditions to be predicted. In addition, the same work contains an exhaustive survey of the changes undergone by heterocyclic and bifunctional compounds, while the systemization and original treatment of these subjects is in itself a most valuable contribution to science. The systematic work on the thermodynamic and kinetic study of the interconversion of rings and linear polymers begun by A. A. in 1950 was a continuation and development of the theoretical considerations presented in the dissertation. This work has been carried out by workers from the organic synthesis laboratory of the VNIIV and the thermodynamic laboratory of Moscow State University.

One of the factors determining the different tendency of heterocyclic compounds to polymerize is the strain in the ring in question. Considerable interest is attached to the measurement of the magnitude of this strain in different heterocyclic compounds. The magnitudes of the strains were previously known only for cycloalkanes with 3 to 8 atoms in the ring. The interconversion of rings and cyclic polymers was studied by A. A. and coworkers in the lactams and cyclic acetals with 5 to 8 membered rings. The strain in the rings was determined by thermodynamic methods: by indirect determinations of the difference in the heats of combustion of the cyclic compounds and the linear polymers, by comparison of the experimentally determined heats of combustion of the cyclic compounds with the value of the thermal effects of the polymerization reaction, calculated according to the additivity principle, and also by study of the equilibrium states in polymerization conditions. The wealth of experimental material obtained in this work confirmed the accuracy of A. A.'s original idea that the strain in a ring is indeed one of the factors determining the reactivity of a given ring and in particular, its tendency to polymerize. The thermal effect and the reaction mechanism of the polymerization of heterocyclic compounds in the presence of different activators were established from a calorimetric study of the kinetics of the polymerization of caprolactam and oenantholactam.

In 1949 A. A. Strepikheev published work on the structure of the higher carbohydrates in which, starting from the general theory of the conversion of rings and linear polymers, he revealed an entirely new view of the structure of polysaccharides and their formation in nature. A. A. suggested that the molecule of the polysaccharides is not unalterable. In the conditions under which rupture of the glucosidic bonds takes place, two competing reactions are possible—rupture of the internal glucosidic bridge of the δ-glucopyranose and opening of the glucosidic bond. As a result of this, the polysaccharide macromolecule may contain, in addition to the glucopyranose residues, hydrated elementary links with an open chain, whose further rearrangement is determined by the relative probability of intra-and intermolecular reactions of the glucoside hydroxyl group.

The conception of hydrated elementary links in the polysaccharides enabled A. A. to put forward a hypothesis of the mechanism of polysaccharide formation in nature by the conversion of the unstable cyclic γ-forms of the monosaccharides into the corresponding polysaccharides.

The experimental data obtained in the study of the comparative strain in γ-and δ-forms of the sugars have shown that, as in the case of other cyclic acetals, the γ-form (i. e. the five-membered ring) of the sugars is more strained than the δ-form (the six-membered ring) of the sugars. This explains the difficulty of isolating the

δ-form of the sugars in the free condition and may provide confirmation of the suggestions made by A. A. concerning the mechanism of polysaccharide synthesis in nature.

In addition to his great scientific research work, A. A. Strepikheev devoted considerable attention to teaching activities and earned the affection of young people. A. A. began his teaching work in 1932 in the Lenin Polytechnic, where he gave a course in carbohydrate and cellulose chemistry. In 1938 he moved to the Chair of Artificial Fibers in the Mendeleev Chemical and Technological Institute, Moscow, and then to the Moscow Textile Institute, where he gave a course on the chemistry of high-molecular compounds. This course was founded by him and became wider and more complete every year. His death prevented A. A. from completing work begun on the creation of a text-book on the chemistry of high-molecular compounds, in which a systematic presentation of the fundamentals of this science were to have been given for the first time.

The memory of Aleksandr Aleksandrovich Strepikheev—talented research worker, great scientist, outstanding engineer, fine comrade, modest, sympathetic, and excellent man—will always remain bright in the minds of all those who knew and worked with him.

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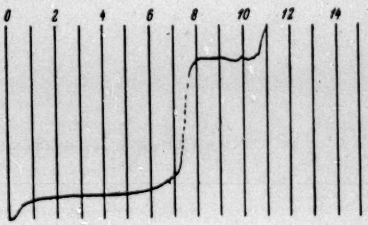
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